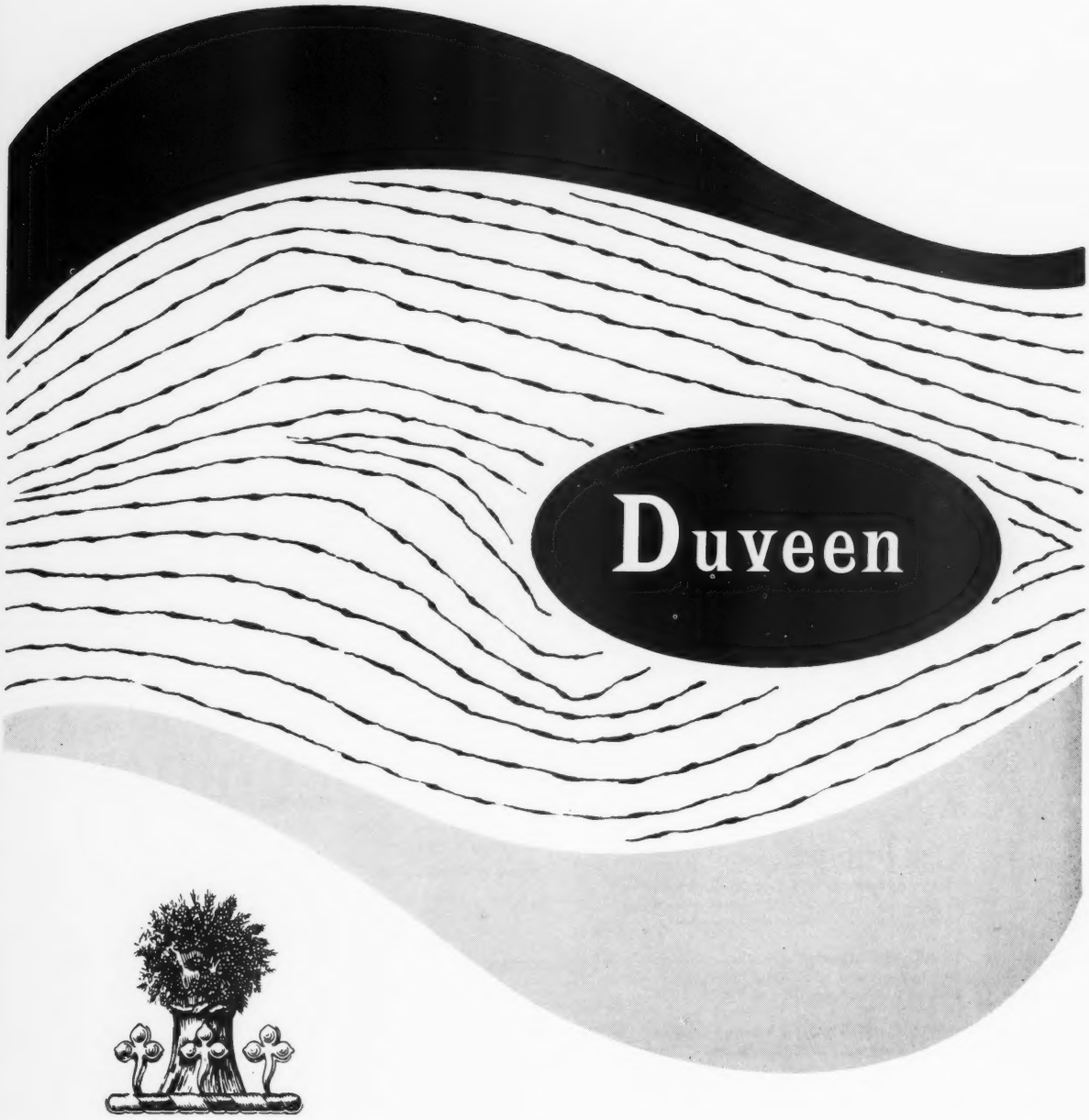


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# Drug and Cosmetic Industry

**Contents** **April 1957 Vol. 80 No. 4**

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*"Do you think 'Happy Pill Bubble Bath— It Tranquilizes' would get by the FDA?"*

# Keeping Posted

### T.G.A. Meeting

The 22nd annual convention of the Toilet Goods Association, being held at the Waldorf-Astoria Hotel, New York, May 7, 8, and 9, will have an overall theme "personality-Key to Future Profits," which will be expressed in the keynote address at luncheon Tuesday, May 7, by Otis L. Wiese, editor and publisher of McCall's. Taking as his topic, "The Changing Personality of Our Times," Mr. Wiese will set the background for the entire convention by exposing the underlying forces that shape the personality of America today and strongly affect the cosmetic market.

The convention will open on the morning of May 7 with the annual address of the President, Pierre Harang, vice-president of Houbigant Sales Corporation; followed by the report of executive vice-president of Houbigant Sales Corporation; followed by the report of executive vice-president S. L. Mayham, report of the treasurer, and the election of officers and directors.

The afternoon of May 7, and the morning and afternoon of May 8, will be devoted, respectively, to sessions on packaging, distribution and promotion, and the manner in which each of these can help build the unique personality of a particular product. Convention chairman, J. I. Poses, of D'Orsay Sales Corporation points out that "an unusual feature of the three panel discussions is the use of a 'jury box' filled with a group of other distinguished repre-- sentatives of the toilet goods industry, a different group for each subject. Members of the 'jury' will question the speakers on each subject. Seventeen leaders will serve on these 'juries' bringing to the convention a greater wealth of speaking talent than it has had in the past."

"What Women Want in a Toiletries Personality," will be the subject of a talk given by Florence Goldin, of Grey Advertising, on the opening afternoon. This will be followed by "personality and Your Package", under the chairmanship of Jack Cawley, and with the following panel members: Kay Brown, Yardley of London—"Packages and Women"; Donald Deskey, package designer—"Product Personality in Your Package Design"; Lloyd Stouffer, Modern Packaging—"New Packaging Trends".

The May 8 morning session will be on "The Changing Personality of Toiletries Distribution. Under the chairmanship of Jean Depres, Coty, Inc., the panelists will be: Ade Schumacher, Liggett-Rexall Drug Stores—"Changing Personality of Today's Drug Store"; Dr. Herman Nolen, McKesson & Robbins—"Changing Personality of the Drug Wholesaler"; Joseph Handleman, Handleman Drug Company—"Changing Personality of Today's Super Market"; Phillip Schindell, Limited Price Variety Association—"Changing Personality of the Variety Store"; John Strauss, R.H. Macy & Co.—"Changing Personality of the Department Store".

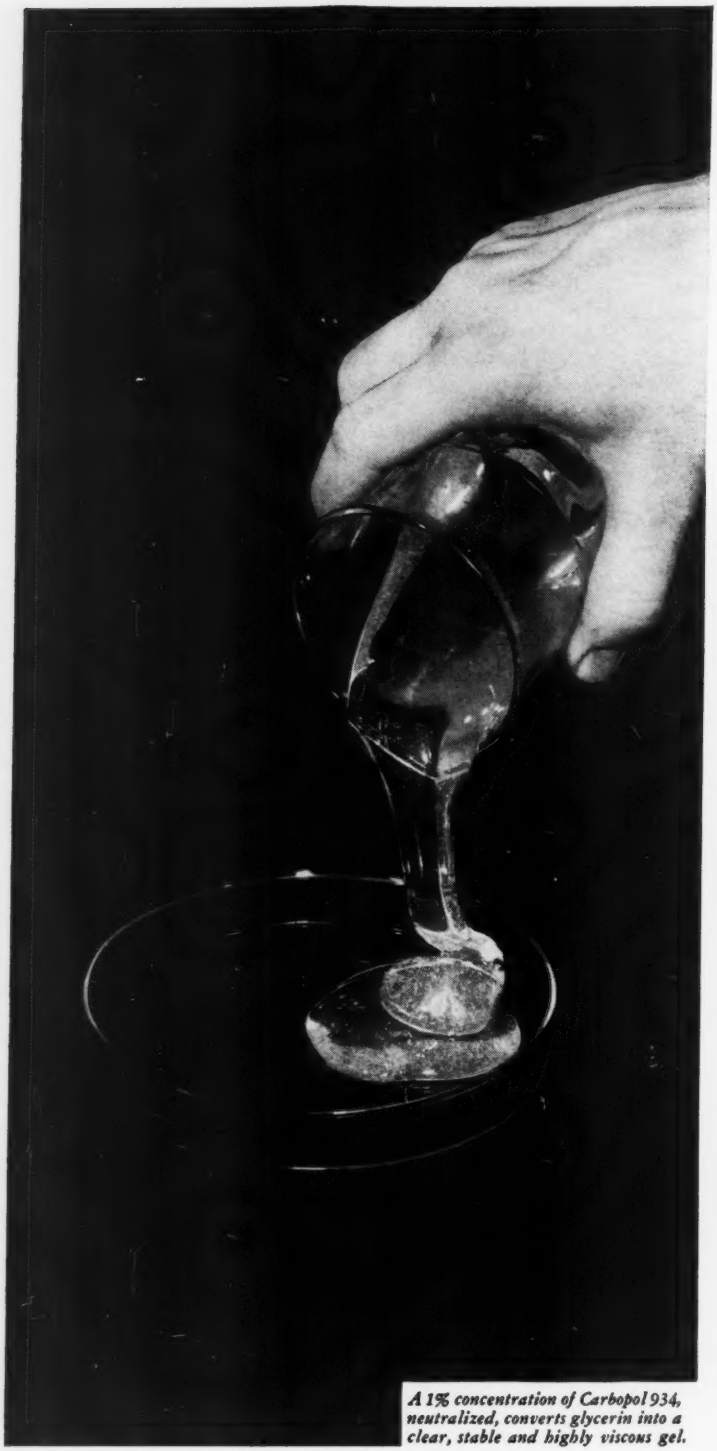
The final business session on the afternoon of May 8 will be on "Building a Product Personality Through Promotion." Under the chairmanship of Donald Bryant, Warner-Lambert Pharmaceutical Co., the panel members will be: Donald Frost, of Bristol-Myers Company, and Norman Mack, of Peck Advertising—"Personality in Advertising"; Janet Myers, Bourjois, Inc.—"A Personality for Tomorrow".

The third day of the convention, May 9, is given over to the meeting of the Scientific Section of the T.G.A. This is under the direction of the Section Chairman Orville Davenport, Avon Products, Inc., and Harold D. Goulden, Scientific Director of T.G.A. The papers to be presented at the morning session are:

Interference of Non-Ionic Emulsifiers with Preservatives V Chromatographic and Chemical Investigation, by Constance Hall and Maison G. de-Navarre, Cosmetic Laboratories, Inc., Division of Beauty Counselors, Inc.; The Measurement of Consumer Reaction to Fragrances, by Noel Schwartz and Dean Foster, U.S. Testing Laboratory; The Antibacterial Activity of the Alumin Salts, by Irvin H. Blank, Ph.D., Department of Dermatology, Massachusetts General Hospital, Harvard Medical

*News about*

# B.F.Goodrich Chemical *raw materials*



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School, and Majories Moreland, M.S., Summit Diagnostic Laboratories, Summit, N.J.; Ethanolamines in Topical Preparations, by John H. Draize, Francis X. Wazeter, and Elsie A. Kelley, Division of Pharmacology, Food and Drug Administration, Bureau of Biological and Physical Sciences, Washington, D.C.

Papers at the afternoon session will be: Pitfalls in Evaluating the Safety of Cosmetics, by Bernard E. Conley, Ph.D., secretary, Committee on Taxicology, American Medical Association; The Analytical Chemistry of Silicones in Cosmetics, by A. Pozefsky and M.E. Grenolble, General Electric Company, Chemical and Metallurgical Division, Silicone products Department; Practical Measurements of Epidermal Emolliency and Emollient Penetration, by Herbert J. Spoor, Ph.D., M.D.

### Rules for Proprietaries in N.J.

Judge John D. Lynn in the Bergen County (N.J.) District Court ruled against the Board of Pharmacy of the State of New Jersey, and in favor of Honey Dew Food Stores, in a suit brought by the Board to prohibit the sale of certain drug preparations in other than drug stores. The products involved are: Vick's Va-Tro-Nol, St. Joseph Aspirin for Children, Phillips Milk of Magnesia Tablets, Anacin, Aspergum, Carter's Little Liver Pills, Bromo-Seltzer, Bromo-Quinine, Alka-Seltzer, Castoria, Ex-Lax, Sal Hepatica, Pepto-Bismol, and Bufferin.

Pertinent excerpts from the decision follow:

"Shorn of legal verbiage and statutory terminology the questions presented for decision are as follows:

1. Are the first named fourteen products involved in this trial "non-poisonous patent or proprietary medicines" within the meaning of R.S. 54:14-29 and therefore excepted from the interdiction imposed by the statute, or are they in the category of poisonous drugs or medicines within the interdiction?

2. If the plaintiff has the right under the pharmacy Act to restrict sales of these fourteen products to registered pharmacists and registered assistants of the State of New Jersey, is the Act unconstitutional under the State and Federal constitutions?

3. If the exception expressed in R.S. 45:14-29 of the Pharmacy Act is not interpreted so as to permit sales of said products by one who is not a registered pharmacist or registered assistant, is the Act unconstitutional under the State and Federal constitutions?

"The Court is satisfied, from the proofs, that each of the fourteen products involved in this case is a patent or proprietary medicine within the meaning of the term expressed in the statute and so finds as a matter of fact.

"It appears quite conclusively that there is no casual relationship between the ingestion of excessive amounts, or the improper use, of the products under examination and the manner in which they are purchased or the place where the purchase is made. The fact is that all control over the usage and dosage of a patent or proprietary medicine, such as those with which we are dealing, ceases with the completion of the purchase and the delivery of the medicine across the counter. It matters not whether the drug or medicine is purchased in a drug store or on a corner grocery; the fact is that, when the purchaser walks out of the store, all control over the drug or medicine passes from the seller and from that time on the responsibility for proper usage lies entirely with the purchaser.

"After having reviewed and considered the entire record of the trial and having had the benefit of the briefs and arguments of counsel, the Court is of the opinion and finds as a matter of fact that the defendant has established by a fact or preponderance of the credible evidence that the fourteen products or compounds under examination are non poisonous patent or proprietary medicines and therefore within the exception expressed in R.S. 45:14-29.

"In view of the foregoing disposition of the first and basic issue before the Court, any further consideration of other issues involving the constitutionality of the Pharmacy Act is unnecessary."

### Grove Cited on Fitch Discounts

Grove Laboratories has been charged with discriminating unlawfully among its customers in the sale and distribution of Fitch hair and scalp preparations. The first of a two-charge complaint brought by the Federal Trade Commission charges Grove with discriminating in price between different wholesale customers in violation of Section 2(a) of the Robinson-Patman Amendment to the Clayton Act. It is charged that some wholesalers receive, in addition to the customary 15 per cent discount, a 10 per cent discount, designated as a "warehouse allowance."

The second count charges that some retailers, in order to buy directly from the company, are required to buy at least specific minimum quantities, while favored retailers may purchase directly in any quantity they desire. This practice, the complaint says, supresses competition and is an unfair competitive method in violation of Section 5 of the FTC Act.

### Cosmetic Chemists Special Award

The Special Award for outstanding scientific literature, presented annually by the Society of Cosmetic Chemists, and carrying a prize of $1,000, will be awarded this year jointly to Nobel laureate A. J. P. Martin and co-author P. T. James for contributing an important tool to cosmetic science—gas-liquid chromatography. The two distinguished English scientists will attend the meeting of the Society at the Hotel Commodore, New York, May 10, to receive the award.

Publications by Dr. Martin and Dr. James on gas-liquid chromotography represent an outstanding advance in basic knowledge, according to the SCC Literature Review Committee which reviewed fifty-five recent publications in fields related to cosmetic science. The Committee pointed out that "Gas-liquid partition chromatography opens the way to basic information concerning the composition of natural products and processes. Martin and James have applied it to the study of fatty acids, amines,

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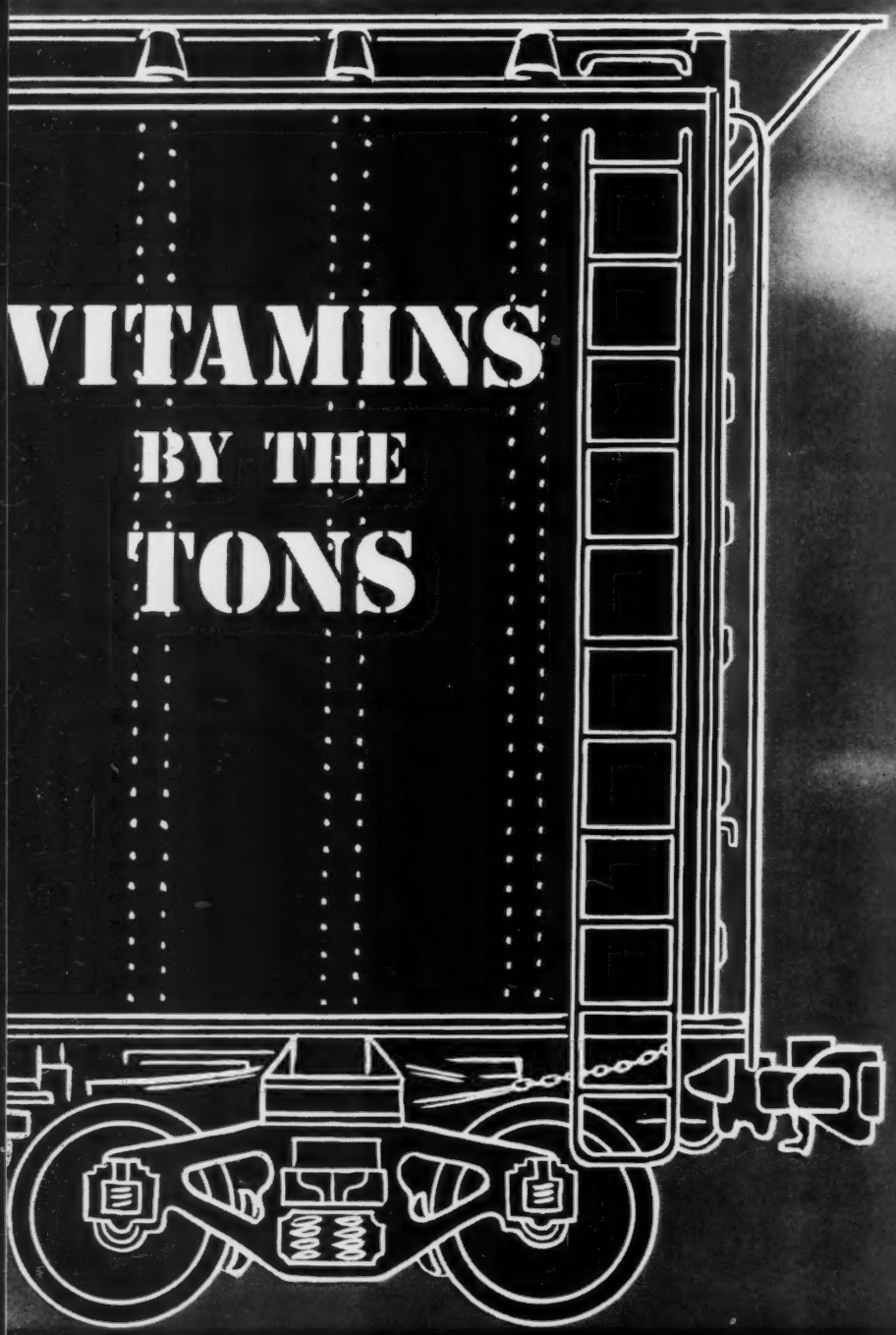


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and hydrocarbons. James' article on sebum illustrates how valuable it is in investigating a biological fluid. Gas-liquid chromatography shows great promise as a tool in cosmetic research and has already contributed to advances in aerosol and perfume technology."

Dr. Martin mentioned the development of gas-liquid chromatography in his speech at the 1952 Nobel Presentation. Dr. Martin and his co author, Dr. Richard L. M. Synge, were awarded the Nobel Prize in chemistry for the development and application of partition chromatography. A Fellow of the Royal Society, Dr. Martin also holds the Berzelius Gold Medal of Sweden. He heads his own scientific organization and is continuing the development of gas chromatography.

Dr. James is at the National Institute for Medical Research, studying fat metabolism. Before joining Dr. Martin at the National Institute in 1950, he was associated with Dr. Synge at Lister Institute.

### Sterling to Enter Biologicals

Sterling Drug Inc. will enter the field of biological products for the first time in its history. A substantial expansion in the research program of the Sterling-Winthrop Research Institute, Rensselaer, N. Y., which is the research center for all Sterling subsidiaries and divisions, will bring the company into biologicals, including vaccines, for the treatment of virus diseases.

Sterling Drug Board Chairman, James Hill Jr., said that major increases are slated in the Institute's biological research facilities which are devoted to chemotherapeutic and physiological studies of the action of new medical preparations. Additionally, he announced a new product development building to be erected on the Institute's 70-acre site to work out the chemical processes required for the economical, large scale manufacture of new pharmaceutical products. The Institute's expansion in research and the production of biologicals to treat virus diseases reflects the increased medical and scientific interest in vaccines as well as the Institute's own research progress in this field, Mr. Hill said. A number of biologicals for human and veterinary use have been developed by the Institute to the stage where they are now ready for clinical testing.

### Drug Financial Ratios

In analysis of the figures of 42 drug manufacturers for 1955, Dunn & Bradstreet report the following ratios: Net profits on sales, median 8.72, upper quartile 11.44, lower quartile 3.50; net profits on tangible worth, median 15.25, upper quartile 24.87, lower quartile 8.42; net profit on working capital, median 27.50, upper quartile 38.14, lower quartile 15.76; net sales to tangible worth, median 2.01, upper quartile 2.56, lower quartile 1.32; net sales to net working capital, median 3.13, upper quartile 3.79, lower quartile 2.37; collection period, median 41, upper quartile 33, lower quartile 53; net sales to inventory, median 5.9, upper quartile 7.5, lower quartile 3.6; fixed assets to tangible net worth, median 39.2, upper quartile 25.2, lower quartile 51.8; current assets to current debt, median 3.02, upper quartile 4.96, lower quartile 2.53; current debt to tangible net worth, median 28.5, upper quartile 19.6, lower quartile 39.6; total debt to tangible net worth, median 59.4, upper quartile 43.2, lower quartile 75.0; inventory to net working capital, median 58.2, upper quartile 43.5, lower quartile 76.6; current debt to inventory, median 79.4, upper quartile 53.3, lower quartile 111.7; funded debt to net working capital, median 39.8, upper quartile 24.2, lower quartile 34.4

### Squibb to Retain Brooklyn Plant

Plans of E. R. Squibb & Sons to abandon the Brooklyn plant in favor of a consolidated plant in New Brunswick, N. J., have been dropped. Squibb's industrial relations manager so notified John Heza, president of Local 14-138 of the Oil Chemical & Atomic Workers AFL-CIO and his committee, saying in part:

"This decision should be good news to the employees at the Brooklyn plant. Since the consolidation announcement was made last October there has been an intensive study applied to the problem indicating the possibility of more effective use of existing facilities which makes consolidation unnecessary."

The change in plans makes possible the continued operation of an existing facility with employees skilled in the particular type of production in Brooklyn, it was pointed out. Approximately 1,200 employees would have been affected by the change.

### Armour Research to Kankakee

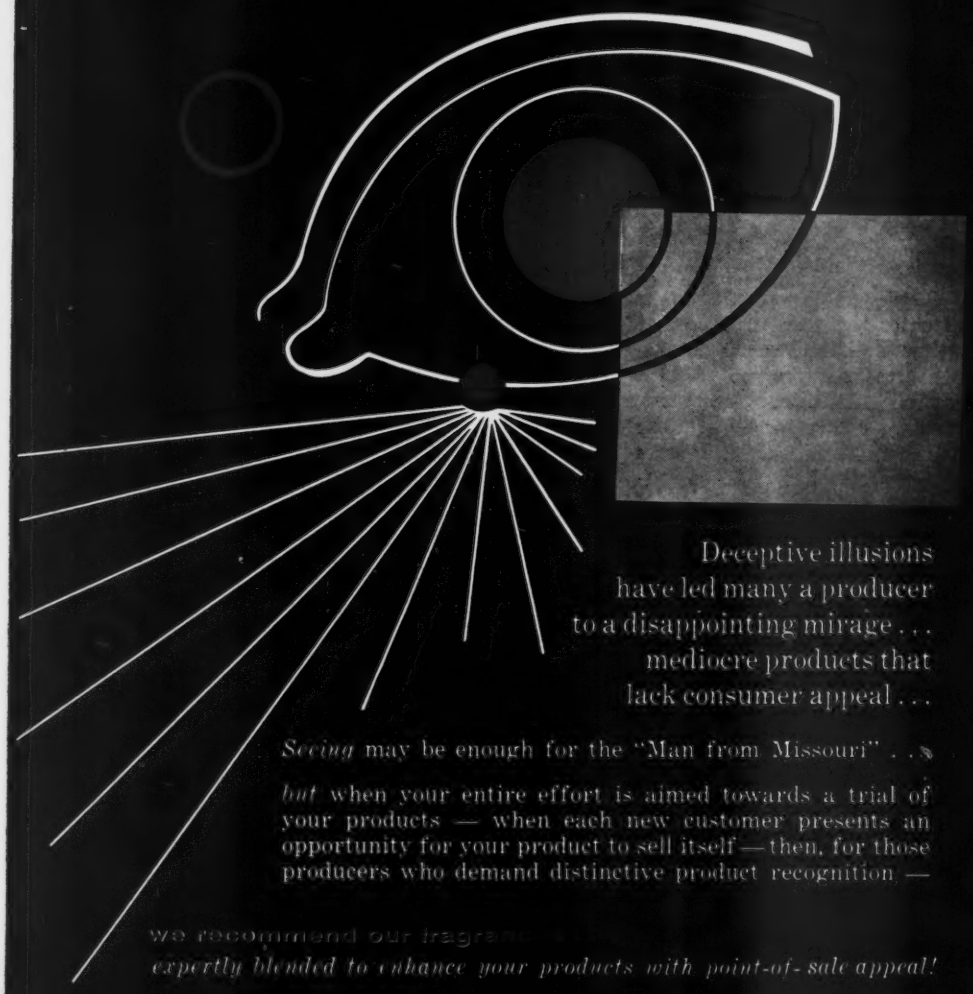
Transfer of the pharmaceutical research operations of The Armour Laboratories from Chicago to the Kankakee plant has been completed. This brings pharmaceutical research under the same roof with pilot plant, medical, control and production facilities along with sales and administrative offices. A relocation of several departments was necessary to accommodate some 35 highly skilled research workers under the direction of Dr. J. B. Lesh, Director of the Pharmacy, Pharmacology, Biochemistry, and Organic Chemistry departments. New drugs are submitted to the Pharmacology Department for screening, a detailed study that may last from two days to two years. At present muscle relaxants, anti-fungal agents, and nutritional products are of primary interest to these investigators. This department includes a pathology laboratory where technicians study tissue sections for changes caused by new drugs. Modern ultraviolet and infrared equipment feature the Organic Chemistry laboratory where the chemical structure of chemical compounds is determined through use of various physical and chemical techniques.

### Drug Wholesale Sales

Drug wholesaler sales in the United States totaled $2.2 billion in 1954, according to the U.S. Department of Commerce. Of these sales, $1.3 billion was reported by the general-line drug wholesalers, and, $0.9 billion by speciality-line wholesalers. In addition, manufacturers of drug preparations reported sales of $883 million through their sales branches and

seeing . . .

is NOT believing!



Deceptive illusions
have led many a producer
to a disappointing mirage . . .
mediocre products that
lack consumer appeal . . .

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sales offices. Ninety-four per cent of the sales of general-line wholesalers consisted of drugs and druggists Sundries, including pharmaceuticals, biologicals, medicines, toiletries, cosmetics and sundries, while the remaining 6 per cent was made up of a variety of commodity lines. The portion of total sales accounted for by drugs and druggists sundries varied by geographical divisions from a low of 88.6 per cent in New England to a high of 97.5 in the Pacific states.

Compared with 93.9 per cent for general-line wholesalers, specialty-line wholesalers had a sales percentage for drugs and druggists sundries of only 88.3 per cent, while 11.3 per cent of the sales of these wholesalers was made up of other commodity lines. Here also, the percentage of drugs and drug sundries varied considerably by geographic divisions, from a low of 69.8 per cent in the South Atlantic states, to a high of 94.0 in the East North Central states.

## Flavoring Extract Meeting

The Flavoring Extract Manufacturers Association, meeting on May 19 to 22, at the Hotel Roosevelt, New York, has announced its program formulated under the direction of Robert Krone, Fritzsche Brothers, chairman of the Convention Committee. Dr. Robert A. Osborn, Division of Food, Bureau of Biological and Physical Sciences of the Food and Drug Administration, Washington, will speak on The Establishment of Standards of Identity for Foods under the Federal Food, Drug, and Cosmetic Act. Ralph E. Burgess, chief economist, American Cyanamid Company, will consider present and future business conditions and discuss problems facing business. Bernard L. Lewis will speak on vanilla publicity. Dr. Bernard L. Oser, Food Research Laboratories, will talk about The Role of Flavor Compositions in the Current Food Additive Situation. Arthur T. Schramm, National Aniline Division, Allied Chemical & Dye Corporation, chairman of the committee representing color manufacturers in the endeavor to seek changes in laws to permit continued use of certified colors on a more realistic basis, will speak on Certified Colors—Facts Behind the Headlines.

Other important talks will be The Vainilla Bean Market, by Ray Schlotterer, executive secretary of the Vanilla Bean Association; the Annual Report of John Hall, executive secretary and general counsel of the F.E.M.A.; Report of the Scientific Research Committee by Dr. A. S. Wendt, Fred Fear & Company; Report on Vanilla Research by Dr. George McNew, Boyce Thompson Institute; Report on Organic Acids in Vanilla by R. Way, Crescent Manufacturing Company; and Report of the Food Additive Committee by Harold Janovsky, Fritzsche Brothers.

Entertainment includes the Suppliers' Hospitality Party on Sunday afternoon, May 19; Golf Tournament at Baltusrol Country Club on Monday following the meeting; a luncheon in New York, followed by afternoon activities for non-golfers; Dinner and entertainment at the Latin Quarter Monday evening; President's Reception and Dinner Dance Tuesday evening; Chemists' Breakfast Wednesday morning.

## Cosmetic Sales Set New Record

A new record for the sale of perfumes, cosmetics, and other toilet preparations, excluding toilet soaps, was established in 1956 when sales at retail totaled $1,321,000,000, an increase of 10.8 per cent over sales for 1955, according to the Toilet Goods Association.

While the increase extended pretty generally throughout the entire list of products, dentifrices, which normally register an annual gain of 5 per cent, showed an increase of 10.5 per cent for last year. Incidentally, dentifrice sales in food stores increased more than 16 per cent. Shaving preparations registered almost the same type of picture with respect to outlets with food store sales gaining substantially over those of other outlets. The total increase was about 9 per cent with aerosol products accounting for by far the greater portion of this gain.

Business in make-up items showed a gain of 14 per cent, due principally to the impact of heavy promotion by leading companies in the field, continues T.G.A. The increase in hair preparations as a general class was less than during the last two or three years but still was a substantial 12.5 per cent. Sales of deodorants increased by nearly 20 per cent with the male market predominating in the rate of increase.

Fragrance products as a whole lagged but did show a slight increase over 1955, all of which was due to increased sale of colognes and toilet waters. Some houses registered a fairly sharp gain in perfume sales approximating the ten per cent shown by the industry as a whole but this pattern was very irregular and a considerable number of houses lagged far behind.

Every type of outlet showed some gain in total sales but the gain in several categories was below the overall percentage of increase; in fact, only one classification of store showed an increase substantially above the national average and that was the food stores whose percentage moved up to 19.1 per cent of the total or an increase of 18.5 per cent above 1955.

Independent and chain stores still lead as the largest outlets but their percentage declined slightly to 29.3 per cent.

| | Chain & Independent Drug Stores | Dept. Stores & Specialty Shops | Food Stores | House-to-House | Ltd. Price Variety Stores | All Other Outlets |
|---|---|---|---|---|---|---|
| 1950 | 37.0% | 27.0% | 6.1% | 14.0% | 11.0% | 4.9% |
| 1951 | 36.0% | 25.5% | 8.5% | 16.2% | 10.0% | 3.8% |
| 1952 | 34.5% | 22.0% | 14.0% | 17.5% | 8.5% | 3.5% |
| 1953 | 32.0% | 22.1% | 15.5% | 18.3% | 8.4% | 3.7% |
| 1954 | 30.2% | 22.5% | 17.1% | 19.4% | 7.5% | 3.3% |
| 1955 | 29.4% | 22.3% | 17.9% | 20.0% | 7.3% | 3.1% |
| 1956 | 29.3% | 21.6% | 19.1% | 19.6% | 7.2% | 3.2% |

## Pfizer Annual Report to Public

Chas. Pfizer & Co. has undertaken another "First" in its business activities. The annual report of the company is being distributed directly to a very large number of people throughout this country,

whether or not these people are stockholders of the company. The report, which was first mailed to stockholders, has been published as a special supplement of the New York Times on Sunday March 31, and of the Chicago Tribune and the Los Angeles Times on Sunday, April 14. The combined circulation of these three newspapers, published in the country's three most populous cities, is over three and a half million. The newspaper edition is identical in format and content to the one mailed March 15 to stockholders. The report contains 16 magazine-size pages. Eight of them, including the front and back covers, feature four-color illustrations.

In addition to the message to stockholders from President McKeen, statement of financial position, consolidated earnings statements ordinarily found in such annual reports, there are several feature articles dealing with special phases of the company's business. Among these is a report entitled "The Health Team Behind Modern Medicine," which describes the teamwork of doctors, pharmacists, manufacturers, and researchers in making available today's drugs.

As to the purpose of this widespread distribution of its report, President McKeen said: "The report plays an important role in dissemination of product information, in our personnel recruiting activities, and in our overall public relations program. Considering the fact that we are making multiple use of a single preparatory effort and a single press run, we feel that we have ecomically achieved a number of important shareholder and public objectives. "It is our hope that this report will not only benefit Pfizer but will also be reflected in a better public understanding of how our corporate free enterprise system operates."

## SKF Research Realignment

In a major extension of its policy to relieve scientific talent of as many administrative duties as possible, Smith, Kline & French Laboratories has freed four of its most experienced scientists for roles as "strategists" in the company's expanded research program. Three of the four—Drs. A. E. Heming, E. J. Fellows, and G. E. Ullyot—have been transferred form SKF'S Laboratories Department, where they had responsibilities over specific scientific disciplines, to Research Operations, where they will be associate directors of research in specific program areas. They will join the staff of Dr. J. K. Clark, director of research.

The fourth scientist, Dr. R. H. Blythe, has been appointed director of pharmaceutical research, a new position which will enable him to serve as SKF's top strategist in that specific discipline. A scientific advisory board, headed by Dr. C. W. Scull, director of development in SKF's Research and Development Division, will assist Dr. Blythe. In turn, Dr. Blythe will serve as consultant to the Pharmaceutical Chemistry Section. Dr. Blythe, who has been with SKF since 1934 when he organized the pharmaceutical laboratories, has been pharmaceutical laboratories director since 1951. Dr. Ullyot, director of SKF Chemical laboratories since 1950, has been with the firm since 1937. Dr. Fellows, director of SKF's Biological laboratories since 1950, is Associate Professor of Pharmacology at Temple University, Philadelphia, and is guest lecturer on the regular staff of the University of Texas' Medical Branch, Galveston. Dr. Heming has been head of Biochemistry Section since joining SKF in 1948, previously being chief chemist for Johnson & Johnson in Brazil and Argentina.

Succeeding Dr. Heming as Biochemistry Section head is Dr. E. E. Van Loon, who came to SKF in September 1955 from the Veterans' Administration Hospital, Louisville, Ky., where he was Chief of the Medical Research Laboratory

## New Drugs Over-the-Counter

Opposition to proposals to allow the sale of some of the newer drugs over-the-counter continue to come from representatives of retail pharmacy. The latest move is that of the New Jersey Pharmaceutical Association in opposing proposals by the Food and Drug Administration that Lilly's Tuamine Nose Drops and Squibb's Spectrocin-T Neomycin Troches be transferred to over-the-counter status as requested by Lilly and Squibb.

The principal reason for the objection to the proposals, according to the complaint of the association, is that the average consumer does not read labels and warnings, and therefore, it is contended, all products which include warning statements in the labeling should be sold only on physicians' prescriptions.

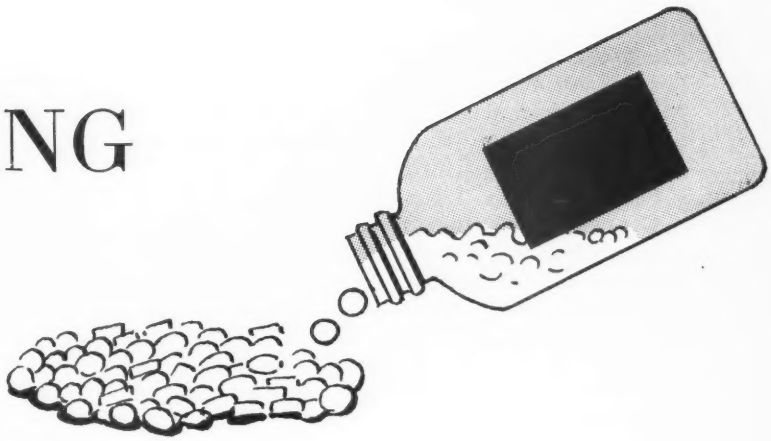
Such an objection has no validity whatsoever. The main consideration is that the preparations sold over the counter should be safe to take if taken in accordance with the directions indicated in the labeling. However, organized retail pharmacy will continue to bring all the possible pressure to bear upon authorities in order to keep the distribution of the greatest number of drug products exclusively in the hands of the registered pharmacists. And while certain factors in retail pharmacy have accused the drug manufacturers of ignoring the safety of public health in their attempts to obtain wider distribution of some types of drug products, one can be quite sure that organized retail pharmacy has no consideration for the welfare or convenience of the public in trying to monopolize the sale of as many drug products as it can.

## Society of Flavor Chemists

The society of Flavor Chemists will hold a Luncheon and Flavor symposium following the close of the annual meeting of the Flavoring Extract Manufacturers Association at Hotel Roosevelt, New York, May 22. The program will include Dr. J. H. McGlumphy, van Ameringen-Haebler, Inc., on Application of the Maillard Reaction in Development of Flavors; J. Broderick, Lever Brothers Company, on Origin of Flavor; Ernest Polak, Polak's Fruital Works, on Biosynthesis of Essential Oils. Information and luncheon tickets may be obtained from the secretary of the Society, Fred Schumm, Ungerer & Co., Totowa, N. J.

# REGULATING New Drugs*

*by Frank A. Duckworth*
ATTORNEY FOR CHAS. PFIZER & CO.



## NINETEEN YEARS; ELEVEN THOUSAND NEW DRUG APPLICATIONS; NO REPORTED CASES.

Not quite nineteen years ago, a new concept was introduced in regulating the marketing of drug products, a procedure whereby the government was given authority to review each new drug prior to its sale in the United States. Since that time about eleven thousand new drug applications have been filed pursuant to these requirements. Products so reviewed have materially changed the course of medical practice. They have reduced death rates from pneumonia, rheumatic fever, cerebrospinal meningitis, tuberculosis, and a host of other killing and crippling diseases. At the manufacturers level, the value of shipments of pharmaceutical products increased from $386,000,000 in 1939 to just shy of $2,000,000,000 in 1954, better than a five fold gain. At the same time, the efficiency with which they conquered disease when compared to the price at which they were sold, resulted during this same period of time in a decline in the percentage of disposal personal income expended for medical care. Whereas out of each dollar spent for medical care in 1939, 18.3 cents went for prescriptions, today, less than 14 cents is spent for that purpose. Hospitalized patients are released three days earlier on the average. Our life span has increased almost seven years.

Yet construction of the complicated statutory provisions which created the procedures by which new drugs are reviewed is not to be found in any reported decision, and notices of judgment contain few references to enforcement action based upon alleged violations of the new drug section of the Federal Food, Drug, and Cosmetic Act. Why?

Certainly there is no lack of opportunity for controversy. The statutory provisions, and regulations thereunder, are subject to varying interpretations. Furthermore, practices that have evolved under the Act and regulations, though generally accepted by both industry and government, may, in some instances, have no legal support. Yet the good sense underlying most of these practices, and the flexibility of the Food and Drug Administration in meeting problems, have contributed to a relationship between the regulated industries and the Administration which is conducive of cooperation; not controversy.

It may also be that neither the Administration nor manufacturers of new drugs have felt disposed to test the legal position of the other. Whatever the reason, the result has been the development of a wholesome relationship between the two groups. It is with these effects in mind that comments are here made concerning the legal position of the manufacturer and the government in carrying out their functions regarding new drug products.

The first problem one meets is in determining exactly what is being regulated. The obvious answer is "drugs" and "new drugs". However, the problem is not so easy for although statutory definitions of these terms seem simple enough their application can be confusing.

> Articles subject to "drug" requirements are: "(1) articles *recognized in the* official [compendia] and (2) articles *intended for* use in the diagnosis, cure mitigation, treatment, or prevention of disease in man or other animals; and (3) articles (other than food) *intended to* affect the structure

* Before Section on Food, Drug and Cosmetic Law, New York Bar Association, January 23, 1957.

or any function of the body of man or other animals; and (4) articles *intended—as* components [of the above]." (Emphasis and bracketed words supplied)

At first reading, the definition seems inclusive and fairly specific. However, a number of questions arise in its application.

For instance:

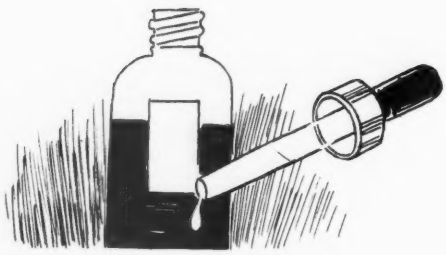
1. Are all articles that are recognized in an official compendium "drugs" even though not intended for drug use; e.g., brandy or water for use as beverages, salt and soda for use as chemical additives to food, antibiotics for use in control of plant diseases, acids and other chemicals for use in industrial operations, etc.? The ludicrous result that would follow a literal interpretation of the statute has been avoided, at least in the case of chemicals for industrial use, by quasi-official exemption, and long standing practices that have not been objected to by the government seem to provide an answer as to the others. However, a cloud upon outright exemption remains in that the drug provisions of the Act might be applicable if such products are not sold in good-faith for other than drug purposes.

2. Another problem under the definition arises in the case of "components" of products intended for drug use. Does the word "components" include intermediates used in the production of chemical compounds for drug use? Chemical compounds, which compose the majority of modern drugs, are far different from mixtures, such as tinctures, fluidextracts, elixirs, etc., which the "component" clause of the drug definition seems to have contemplated. Practice is to distinguish between *intermediates* and *ingredients* but the distinction is one resulting more from the feel of intent than from the language of the statute.

A "new drug" is defined as one which is either not generally recognized as safe for use under conditions prescribed, recommended or suggested in its labeling, or has not been used for a material time or to a material extent under such conditions. What is meant by "material time" or "material extent" or "conditions prescribed, recommended, or suggested in the labeling" is unknown. Legislative history and judicial decision are lacking, and regulations furnish no guide.

Some of the questions frequently arising under the definition include:

1. When does a drug cease to be a "new drug"?
2. Do all similar drug products cease to be "new drugs" at the same time?
3. What effect does inclusion of a drug in an official compendium have upon its status as a "new drug"?
4. Does safety of a veterinary drug depend upon its potential for harming animals or for causing economic loss to the animals owner or for causing harm to human beings who come into lawful or unlawful possession of the drug?
5. What effect does the exemption of a drug from prescription dispensing requirements have upon its status as a "new drug"?



None of these questions has a simple answer. In view of the wide room for controversy, it would seem that conflicts would be frequent and severe. However, outward appearances indicate that the affected industries have felt that the responsibilities flowing from the "new drug" status of a product have not been so burdensome as to require that an issue be made regarding any of the numerous questions arising under the statutory definition.

Having looked at some of the problems arising under the definitions of drug and new drug, we now consider requirements imposed upon new drugs by the statute or regulations.

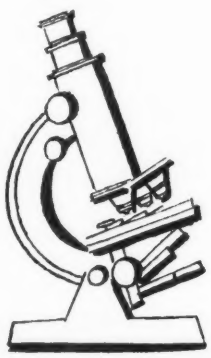
Created in the heat of the so-called sulfanilamide disaster, the quasi-licensing system set up by the new drug provisions of the statute has, from the standpoint of public health protection and economic importance, more far reaching effects than any other portion of this Act or of any other statute, federal or state, regulating drug products.

Under this system, millions of dollars are annually expended by manufacturers in sponsoring the collection of clinical data to form part of the applications that must become effective prior to the marketing of new drug products. Basic manufacturers of new drug ingredients also collect data which is presented to the Administration in the form of a "master file" so that their customers, by referring to such data, may more easily obtain effective applications. An effective new drug application has been likened in value to that of an issued patent. Each year, millions of dollars in sales rest upon the decisions of those in the Administration who review these applications. Although the drug industry and the Administration seem to share with few exceptions a common understanding of procedures under the "new drug" requirements of the statute, when we analyze these requirements, we find that legal support for practices which have evolved is frequently either cloudy or completely missing.

For instance, the question occurs; who must file an application? Must every person who introduces a new drug into interstate commerce file an application, even though an application is already effective with respect to it? The relevant sections of the statute

provide that a violation occurs if one commits the prohibited act of introducing or delivering for introduction into interstate commerce "any new drug unless *an application*—is effective with respect to *such drug*". The statute does not provide that every person who introduces a new drug into interstate commerce must file an application but merely that "an" application must have become effective. Meager legislative history surrounding these provisions furnishes no answer, and the other provisions dealing with new drugs indicate no readily apparent result. Yet the Administration has interpreted the statute to confer a proprietary interest in those holding effective new drug applications, and feels that the only way by which another can benefit from such an application is by the express consent of the person who filed it, or his duly appointed sucessors in interest. Failing to obtain such consent, clinical research must be conducted anew as if the conclusions shown by such research had never been proved. However, the absence of such an interpretation might well lead to a kind of unfair competition where the fruits of costly synthesis and pharmacological screening programs preceding selection of a product, and subsequent toxicity studies and clinical investigations would be reaped by those who lazily lie in wait and, without effort or expenditure, pluck them. Regardless of the legal basis, the good sense in the Administration's interpretation has probably been a major reason for the lack of reported decisions indicating any opposition to it. It may be noted, however, that under the antibiotic certification system, once the Administration has published a monograph based upon clinical and pharmacological data submitted by one manufacturer, others who wish to manufacture the product may do so without submitting such data.

Now let us suppose that a manufacturer has decided to go ahead and file an application, regardless of the fact that other applications are already effective with respect to the drug. How can he best proceed? Of course he may sponsor the clinical work prerequisite to obtaining an effective application anew, and if such is done, an effective application will be issued to him so long as he meets the other requirements. As stated before, the Administration also permits the applicant to arrange with one who holds an effective application, or who has filed a master file containing clinical information, to permit his use of the data contained therein. As to the latter alternative, however, the would-be applicant could search the statute and regulations without any suggestion of how to proceed, or indeed, whether such a plan is even permitted. Again, the Administration's procedures in this regard make sense and seem to be generally followed without serious question.



Another reference procedure is one whereby the applicant files an application supplementary to an effective application, with the consent of the one holding the effective application. Unlike the first procedure where the resulting application is separate and distinct from the one to which reference was made, the second method may give birth to a child dependent upon its parent. Although the second method has been widely used, it is not clear whether the child is affected by any future transgressions of its parent, or whether the parent is responsible for the defelcations of its offspring. However, again no serious difficulties in this regard appear to have arisen, and I hope that I will not be unduly repetitious in pointing out that this is probably due more to the spirit with which applicants and the Administration have approached the matter than to a clear understanding of the rights and responsibilities of the parties.

Carrying our fictional applicant a step further, we find him a successful suitor possessing a quasi-license entitling him to stay at the best hotels. Then he changes his mind and now desires to vary the methods, facilities, controls, or labeling from those set forth in the application. Must he inform the F.D.A. of such changes? If he looks at the statute for guidance, he finds none. However, the Administration has apparently found authority to require such notification, as well as their prior approval, in the statutory grounds for revocation or suspension of an application. That section states that the only grounds for revocation or suspension of an effective application are: (1) subsequent data showing the drug to be unsafe, or (2) an untrue statement of a material fact in the application. The latter was interpreted by regulation to mean that changes in conditions of use, components, composition, methods or facilities of manufacture, processing, or packing, or in labeling would cause the application to contain an untrue statement of a material fact.

An important question, in addition to that concerning statutory support for the regulation, is this: What procedural safeguards, such as right of appeal from adverse decision, and limitation of time upon administrative action or inaction, which the applicant enjoyed in connection with the original application, does he have in regard to his application to make such changes? Does the proposal gain effectiveness by lapse of time, as in the case of the original appli-

*(Continued on page 546)*

*So much has been written of late concerning the potential of lysine as a food and feed supplement on the one hand and of the dangers of amino acids supplementation on the other that the time seems propitious for a careful evaluation of the situation.*

# LYSINE

*by E. E. Howe, Ph.D.*

MERCK SHARP & DOHME RESEARCH LABORATORIES DIVISION
OF MERCK & CO. INC., RAHWAY, NEW JERSEY.

Lysine is a relatively simple organic molecule, L-$\alpha\,\epsilon$ diaminocaproic acid. It is commercially available as the monohydrochloride salt. As far as it is known it must be supplied preformed to all higher animals. The only known compounds which will replace lysine are its *e*-N-acetyl and *e*-N-methyl derivatives.[1] It is unique among the amino acids in that the α-acetyl derivative is not biologically active in rats. Its optical isomer is unavailable to all species tested.

Shortly after the discovery of threonine which enabled him to demonstrate the essentiality of the amino acids, Rose[2] established that rats on a diet containing 18 per cent of amino acids grew optimally when one per cent of the total ration consisted of lysine. Later it was reported that the lysine requirement for optimal growth in chicks is a function of the protein intake.[3] This observation has been extended to include other amino acids and other species.[4] More recently however, evidence has been presented to show that at protein levels from 16 to 32 per cent the lysine requirement of swine is constant.[5] Much more experimental work will be required to establish the effect of such factors as energy content, species differences, and type of protein upon the lysine requirement of animals.

It has been demonstrated that young men under carefully specified conditions require a daily intake of 800 mg. of lysine for the maintenance of nitrogen balance[6] and that the requirement for infants is approximately 90 mg. per kilogram of body weight.[7] It now seems certain that the ratio of lysine to total protein intake must be greater in growing animals of some species than in adults.[8,9] Holt,[7] however, reports the optimum lysine-tryptophane ration to be identical in infants and in man.

## Availability

Lysine is found in relatively high concentration in most animal proteins. The proteins of muscle, milk and blood contain 10, 8.8 and about 9.5 per cent of lysine respectively.[10] On the other hand most vegetable proteins are comparatively deficient in this amino acid. For example, the proteins of corn meal, wheat flour and rice contain 2.3, 1.9 and 3.2 per cent of lysine.[10] It is completely lacking in zein, one of the most important proteins of corn. The proteins of legumes and of grass leaves occupy an intermediate position. Soy bean oil meal, the protein of which contains 6.8 per cent lysine, is often used to supplement other plant proteins.

Some animal by-products such as dried blood have not proved entirely satisfactory for animal feeds and therefore are used extensively as fertilizers. The lysine contained in these raw materials may be conveniently isolated after hydrolysis with mineral acid by suitable ion exchange procedures.[11] It is obvious that should food and feed supplementation become widespread, the supply of such raw material would soon become exhausted.

Numerous methods have been devised for lysine synthesis. One of the most attractive is that devel-

oped in the duPont laboratories using the cheap raw material dihydropyran through the intermediate, polytetramethylenehydantoin.[12,13,14] These same investigators have also worked out an elegant resolution using L-glutamic acid as the resolving agent.[15,16] The residual D-lysine is racemized in good yield by means of a sulfonic acid ion exchange resin at a high temperature and the resultant DL-lysine recycled.[17]

Very recently a fermentation process for the production of lysine has been developed at the Pfizer laboratories.[18] α-Diaminopimelic acid is produced in good yield by a fermentation with a strain of *E. coli* after which without isolation it may be converted to lysine by addition of a decarboxylase containing preparation produced by culturing a second strain of *E. coli* or a strain of *A. aerogenes*.

The preparation of lysine from a natural source, whether it be from fermentation or from plant or animal protein, has the advantage that no resolution is required. L-Lysine monohydrochloride of greater than 98 per cent purity is readily prepared by either method.

The bulk selling price of lysine is now 12 per pound at current levels of production. All the methods described above are capable of producing a lower priced product should the market demand be substantially increased.

## Assay and Standard of Purity

Knowledge of the amino acid composition of foodstuffs affords a method of estimating their biological value. Since lysine is the limiting amino acid in many plant proteins, a reliable method for its determination is especially important. Because the amino acids are structurally so closely related, accurate chemical methods of assay are lacking for many of them. During the last fifteen years very satisfactory methods have been developed based on the absolute requirement of certain microorganisms for the amino acids.[19] A synthetic medium lacking only in the substance to be determined is introduced into a series of tubes and inoculated with a suitable microorganism. Graded amounts of the unknown sample are added and after incubation the amount of growth is determined either by measuring the turbidity of the medium or by titration of acid formed. By comparing the response obtained with the unknown samples with those obtained with graded levels of the pure compound an accurate quantitation can be made.

Classically, specific rotation, elementary analyses and formol titration have been used as criteria of purity of amino acids. Unfortunately, all these standards fail to detect contamination with substances having like properties. More recently it has been shown that the method of solubility analysis is eminently suited for determining the purity of amino acids.[20] By this procedure, the purity of lysine monohydrochloride can readily be established with an error of one per cent or less. A lysine sample, the purity of which has been so established, may be used as a standard for microbial analysis which in replicate is accurate within three per cent and is more rapid and less tedious than the solubility method.

## Lysine Supplementation Human Food

As has been previously stated, the lysine content of cereal proteins is comparatively low. Animal experiments have repeatedly demonstrated that lysine supplementation of certain of these proteins or of the grains themselves, will increase the rate of gain of body weight and improve feed efficiency. Without doubt many cereal proteins supplemented with the proper amount of lysine are better proteins. This is not to say that further supplementation with other amino acids will not improve them still further. It follows, therefore, that any population subsisting substantially on cereal diets will probably benefit from judicious use of added lysine.

In this and other industrialized countries in which the diet is so varied and the consumption of animal protein so great, it is unlikely that any large segments of the populations derived a high percentage of their dietary proteins from cereals. On the other hand, there may be minority groups which do so. Older persons living alone and populations of some of our less well developed areas may consume very small amounts of animal products. Economics permitting it might be worthwhile to fortify cereal products in the United States or Western Europe even though the fraction of the population which derives benefit therefrom may be low.

In very large unindustrialized areas of the world the greater part of the populations do subsist largely on cereal grains. Most of these people would undoubtedly be benefited by lysine supplementation.

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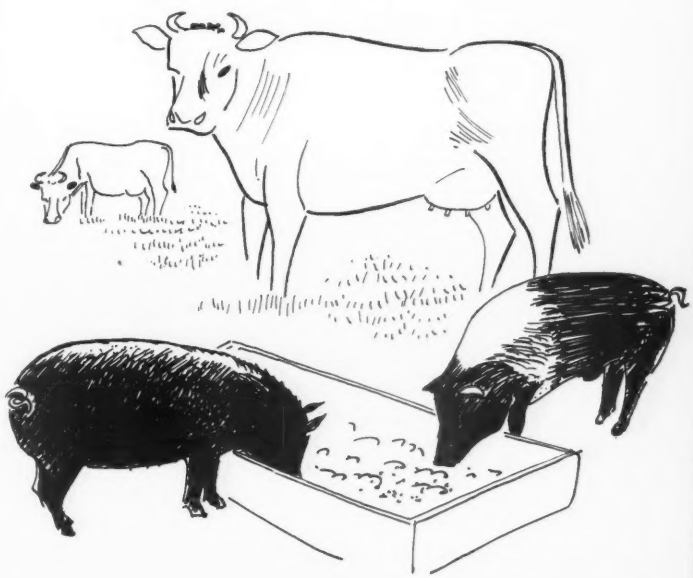


# EYE Make-up *by Harry Hilfer*

Eye Make-up products are not as important as are lipsticks, from a use standpoint but are still a necessary adjunct to a complete make-up line. Their function is to enhance the appearance of the eyes by accenting the eyelashes, eyebrows and the eyelids, thus making the eyes appear larger, bluer or darker in color and in the final analysis prettier. There are three primary classifications of eye make-up products—the mascaras, eyebrow pencils, and eyeshadows, with the mascaras, perhaps being the most important.

Since these preparations are used around the eyes, colorants which may be used are limited to natural colors and acceptable inorganic pigments. Synthetic coloring agents such as the lakes are barred by law. As a result, vivid coloration is difficult to achieve, because of the relative drabness of the permitted pigments. The colors in most common use are the different varieties of carbon blacks—chiefly ivory black—the iron oxide colors, such as the ochers, umbers and red oxides, and the ultramarine blues. These pigments must also come within the permitted tolerances for lead and arsenic content.

Mascaras are usually used on the eyelashes. They must, therefore, be formulated so that they may be easily applied and so that after application the film will be able to withstand aqueous media, such as tears which the eyes may be subjected to. The mascara may, therefore, be regarded as a color incorporated in a vehicle which enables the user to apply it easily and which after application will keep the color in place.

There are several different forms in which the mascara is made, the most common being the tablet applied by means of a moistened brush and the cream type in which the creamy mass is extruded from a tube onto a brush and then applied. The tablet form is the older and, I believe, the more popular of the two. The vehicle used consists of, usually a triethanolamine stearate soap incorporated in a wax and oil mixture—of which carnauba wax is the predominant component. Since triethanolamine soaps are soluble in fixed oils and waxes, solution may be easily effected at higher temperatures. The colors may then be ground in with the help of a roller mill with heated rollers, the mass remelted and poured into molds. The ratio of the soap to the wax determines the ease of application and the ability of the film to stay in place. Too large a wax concentration will make it difficult for an emulsion to form when the tablet is treated with the moistened brush and, therefore, will cause insufficient pickup of the colorant for application by the brush. The reverse—too much soap—will cause the film to be too easily removed by water. The formulator must, therefore, find the point where he can obtain maximum pick-up with maximum protection of the film against water. If the film is found to be too brittle and, therefore, has a tendency

COURTESY GERMAINE MONTEIL

to flaking, the introduction of a liquid wax or a softer wax would be indicated. Carnauba wax was mentioned as being the primary ingredient of the wax portion because its use in this conjunction is well established. It has a high melting point and is extremely resistant to water. In addition, it imparts a highly desirable sheen to the film. In order to soften the film so that there will be no flaking, beeswax is sometimes added as well as spermaceti. More recently the introduction of isoproxyl myristate has given equally desirable results.

If in a given formulation a concentration of triethanolamine soap is used which prevents the mass from melting at a convenient temperature and, if it is also found that lowering the soap concentration as a means of lowering the melting point would spoil the desired application effects, replacement of part of the stearic acid soap with a myristic acid soap could lower the melting point sufficiently. Oleic acid soaps may also be used if there are no prooxidants present as there would be if iron oxide pigments are to be used.

Color concentrations in mascaras vary with the colors that are used. The carbon blacks are usually used in a 10 per cent concentration, but other pigments would probably have to be used in greater concentrations.

The cream mascaras are usually cake mascara to which water is added. In actual practice some formula changes would have to be made in the interests of a stable preparation and it is, therefore, quite common to find auxiliary emulsifiers such as glyceryl monostearate used in this connection.

The water phase usually is about 50 per cent of the formula weight. The advantages inherent in a cream mascara lie in the greater convenience in use—since there is no necessity of forming a cream by trituration with a wet brush and also, in the fact that the manufacturer incorporates the proper amount of water into the cream instead of depending on the customer's

(*Continued on page 532*)

# Time-Intensity Studies

*by Anne J. Neilson,* ARTHUR D. LITTLE, INC.

Good timing is just as important to good flavor as it is to good performances in sports or in the theatre. A flavor chemist tries to create flavors that have a quick favorable impression, which lasts as long as is necessary for that particular product. Sometimes, however, these favorable impressions are upset when one or more components appear at too high or too low an intensity at the wrong time. Sometimes even the whole flavor appears at the wrong time, or lingers too long. In problems as these one helpful means of gauging your success in re-establishing a good balance of flavor is to first prepare a time intensity curve of the problem product, and then using this as a standard compare similar curves of improved products.

A time-intensity flavor study is one that determines a graphical relationship between the strength or intensity of perception of a particular factor, and the length of time this factor is perceived. The factor to be measured can consist of a single taste—the basic taste bitter, for example, or can be a whole flavor complex.

This type of study is used with flavor-by-mouth evaluations only, particularly in cases where a food product has one outstanding, and often unpleasant characteristic which you are trying to mask or control in some other way. With food products where it is desired to have a prolonged flavor, time-intensity studies are most helpful in screening different flavorants to see which is most successful.

In the Flavor Laboratory time-intensity studies are conducted by members of a trained flavor panel familiar with the product under test. As in other flavor studies, this panel is conducted in an odor-free panel room in the same concentrated but unhurried manner necessary for all flavor evaluations. If there is not a clock with a second hand conveniently located in the panel room, one is brought in and placed in such a way that all panel members can see it. The panel leader presents a uniform amount of sample to each panel member, and when all are ready, each one takes the material into his mouth and swallows it immediately. After swallowing, each panel member individually records his observation of the intensity of the factor under test, on a piece of graph paper. Normally, these intensity observations are continued until the characteristic can no longer be perceived. In some cases, however, a predetermined time limit is set and observations are stopped at this point. A composite graph is made of the individual judgings.

The equipment needed for such a test is minimum; namely, a clock or stop watch, and graph paper with time and intensity coordinates. For work in the Flavor Laboratory intensity values are based on a 0 to 3 scale x, threshold; 1, slight; 2, moderate; 3, strong). These numbers are placed on the y-axis. Intervals of time are placed on the x-axis and are marked off in seconds, or in seconds and minutes. Any scale of intensity and time measurements which best suit the product under test may be used, however. In addition to the basic requirements already outlined, it must be remembered that the panel members should be familiar with flavor evaluation techniques, relaxed, and prepared to sit still and diagram one sample for as long as ten to twelve minutes.

As was noted above, one application of this type of test is to measure the intensity and duration of

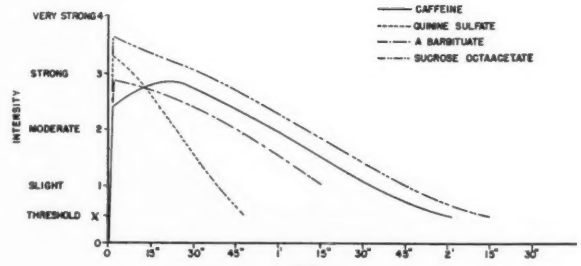


FIG.1 INVENTORY CURVES OF BITTER COMPOUNDS IN WATER

one particular factor. For instance, it has been observed that in tasting various substances which have bitterness as part of the total flavor, the time of perception and the duration of the bitterness may vary from one product to another.

This phenomenon was graphically illustrated when a flavor panel tasted a group of four compounds all known to be highly bitter. An aqueous solution of each compound was prepared with the bitter at the same high level of intensity. The compounds were similar in that they were strongly bitter immediately, with caffeine having a 30 second delay before the peak of bitterness. The duration of the bitter sensation on the other hand varied quite a bit with quinine sulfate having only a one minute duration where sucrose octa acetate which was as bitter to start with, had a two and one-half minute duration. Fig. 2 illustrates a case in which the bitterness quickly reaches a strong intensity but drops off slowly to a low intensity and persists at this level for a long time, as much as two to three minutes. In a more acceptable beer the intensity of the bitterness follows the same pattern of reaching a peak quickly but then disappearing quickly upon swallowing. In this beer the bitterness appears to be part of the over–all flavor sensation as shown in Fig. 2.

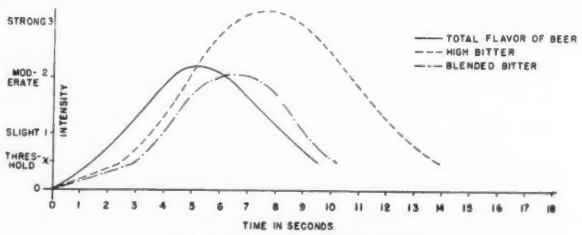


FIG. 2 INTENSITY CURVES OF BITTER IN BEERS

Following this study of isolated bitter tastes, the bitter factor of one particular beverage was studied. It has been found that in beer bitterness is a necessary and desirable characteristic, and a high intensity of bitterness can be tolerated if it is of short duration. However, if this factor lingers too long after swallowing, there is the possibility that the bitterness would cause satiation in the mouth.

Time intensity curves are used also for measuring progress in flavor problems where it is necessary to control a predominate factor. For instance, some drugs in liquid form have only a single impression—they are terribly bitter. In such cases an

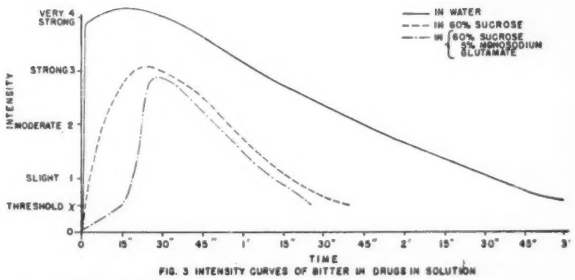


FIG. 3 INTENSITY CURVES OF BITTER IN DRUGS IN SOLUTION

attempt is made to suspend the drug in a flavor complex which makes the bitterness less noticeable. In one particular study it was found that with the drug alone and in water solution, an extremely high bitterness was immediately perceived. This intensity decreased slowly minute by minute but was still noticeable at the end of four minutes. For this particular drug study, panel members first determined the bitter curve of a 0.2 per cent aqueous solution of the drug. Once the standard curve was established, mixtures containing this same dosage were examined. In all cases the mixtures were prepared so that one level teaspoonful contained the required dosage. One sample only was tasted at each panel session, and panels were scheduled four hours apart. It was found eventually that a flavor complex based on feeling sensations was one way to make this high bitterness tolerable. To delay the perception of bitter and to provide a coating for the tongue demulcent action was employed. An aqueous solution containing 0.2 per cent of the drug was mixed with a 60 per cent sucrose solution. The onslaught of bitterness was delayed as the bitterness did not hit a peak for 30 seconds. The duration of the bitterness was decreased to approximately two minutes.

Further, when a material with a great deal of mouth filling sensation as monosodium glutamate was added to this sucrose drug mixture, the perception of bitterness was delayed a full 15 seconds, and the duration shortened another one-half minute. A comparison of the curves in Fig. 3 indicates how effective this combination was.

*(Continued on page 534)*

*High blood pressure or some other cardiovascular trouble affects one out of three Americans. Rare in the below twenty age group, about 60 per cent of elderly folk are afflicted. As infectious diseases succumb to the wonder drugs and life spans increase the demand for effective hypotensive drugs has zoomed. Well over forty million dollars was spent in the past year and the figure will probably surpass fifty million this year. Naturally the multiple uses of drugs such as phenobarbital and reserpine make clear-cut estimates impossible.*

*Defined in many ways hypertension boils down to an abnormal elevation of blood pressure resulting from constricted arteries and arterioles. Therapy aims at restoring statistically normal values.*

# Hypertension Drugs

*by Bernard Idson, Ph. D.*
RESEARCH DIRECTOR, JULIUS SCHMIEL, INC.

Most patients with high blood pressure show no readily determined organic ailment. This is termed essential hypertension, the most common type of heart disease. Arterioles are constricted and the heart must pump harder to supply the body's tissues with blood. The cause of the condition is unknown but present evidence points to the inability of a damaged kidney to deaminate or deactivate pressor amines, especially epinephrine.

The ideal hypotensive drug would be one which stopped constrictor activity and reduced the blood pressure without cutting down the blood supply to vital organs like the brain, heart or kidney. Specifically arterial pressure should be reduced at least 20 mm. Hg., produce no serious side effects, be effective by mouth for lengthy periods, not develop patient tolerance on prolonged administration, and the therapeutic dose should be considerably less than the toxic dose. Lastly but of vital import the control of blood pressure should not vary greatly with the emotional state of the patient. The long-term nature of the illness, with continued use of drugs, makes the price an important factor.

Five years ago there was little the physician could offer except mild sedation, diet and mutilating surgical procedures such as sympathectomy. A series of effective agents have since appeared. While a long way off from meeting all the above ideals they are approaching ever closer. Arterial pressure can be satisfactorily reduced in more than half the patients with currently available drugs according to Dr. Irvine H. Page, president of the American Heart Association. Most impressive results have been obtained in patients with malignant hypertension; with restoration of vision, control of congestive heart failure and prolongation of life. There is now strong evidence that the use of hypotensive drugs, if maintained in such a way as to secure a sufficient degree of blood pressure reduction for a sufficient part of the 24-hour day, leads to a considerable amelioration, often to the disappearance, of the clinical symptons.

## The Drugs

Research into the synthesis of hypotensives has aimed at agents which will have direct or indirect action on the central nervous system (reserpine, veratrum), vascular smooth muscle (hydralazine), and on the autonomic ganglia (hexamethonium, pentolinium, chlorisondamine, mecamylamine).

## Rauwolfia

The most widespread agent for the treatment of essential hypertension is the Rauwolfia Serpentina root and its alkaloids (reserpine, rescinnamine). About 90 per cent of the products on the market contain Rauwolfia or its derivatives, alone or in combination. If dosages are suitably adjusted it makes little difference whether crude root extracts or the purified alkaloids are given. However, reserpine (one of the principal active ingredients) has largely supplanted use of the whole root.

The combination of tranquilizing and hypotensive action has made Rauwolfia aklaloids the almost universal drugs of choice in milder types of hypertension. Usually an interval of two to three weeks

exists between the start of oral therapy and clinical effectiveness. Severe hypertension is treated intramuscularly with an effect produced in roughly three hours with a duration of about ten hours.

Rauwolfia finds its greatest clinical use in combination with other hypotensive agents such as with the more potent ganglionic blocking agents, with hydralazine, and with the Veratrum alkaloids. It helps neutralize the side-effects of these drugs and permits the use of smaller doses of these more powerful drugs. The laxative effect of reserpine often offsets the constipating effect of the ganglionic blocking drugs. Similarly, the cardiac slowing by reserpine often decreases the annoying tachycardia (rapid heart action) produced by hydralazine. In striking contrast to these others, Rauwolfia has a wide margin between the therapeutic and toxic dose.

Despite the success of derivatives of Rauwolfia serpentina in the milder types of hypertension, their use is not without danger. Mental depression is encountered in some patients when kept on the drug for appreciable lengths of time. Nasal congestion, bradycardia (slow heart beat) and increased gastro-intestinal activity are other side complications. The latter is a danger in aggravating a peptic ulcer or producing severe cramps when a colitis is present. These untoward reactions are usually successfully overcome either by combination with small nontoxic doses of ephedrine or a proper antacid. Omission of the drug for short periods of time usually control the side effects. It is necessary, however, to stop the drug if mental depression occurs.

Chas. Pfizer has recently entered the cardiovascular field with "moderil" which contains rescinnamine alkaloid, also derived from Rauwolfia serpentina The company claims appreciably less toxic reactions, as compared to reserpine.

The mechanism of action of Rauwolfia alkaloids is believed to be a displacement of serotonin from receptors in pathways of the corticohypothalamic tracts, causing inhibition of nervous reactions from circulatory spasm. It is interesting, in light of the famous tranquilizing effect of reserpine and its displacing action on serotonin that chlorpromazine (Thorazine), a valuable tranquilizer and also a serotonin antagonist, has little hypotensive value.

### Hydralazine (Apresoline)

(1-Hydrazinophthalazine Hydrochloride)

Hydralazine (Apresoline; Ciba) also affects the central sympathetic nervous system acting directly on vascular smooth muscle to increase renal blood flow, pulse rate and cardiac output. The drug is effective in moderately severe hypertension, but its use is confined to more advanced stages of hypertension combined usually with a ganglionic blocking agent.

Serious side reactions demand extreme care. Headaches, nausea, vomiting, fever, and fluid retention are toxic manifestations. In patients with coronary artery disease, angina may occur or be aggravated. If used alone hydralazine causes a rheumatoid syndrome in about 10-20 per cent of patients who take the drug for a year or more. This danger is eliminated if used in combination with reserpine or with the ganglion blockers.

Recent claims for hydralazine include offsetting the effects of toxemia of pregnancy. Reducing pressure and increased renal blood flow helps mothers with eclampsia and preeclampsia superimposed on essential hypertension.

### Ganglionic Blocking Agents

The most potent and potentially most dangerous hypotensive agents are found in the autonomic ganglion blocking drugs, which block nerve transmission at the autonomic ganglia. Desirable effects of these drugs are due to the interference with sympathetic stimulation. Undesirable effects result from interference with parasympathetic stimulation. Their chief disadvantage lies in their relative unpredictability or uneven control of severe hypertension. They are generally contraindicated in peptic ulcer, coronary disease, recent blood loss and in the presence of poor renal function.

The effective ganglion blockers are hexamethonium (Methium, Bistrium, Hexameton, Esomid, etc.) pentolinium (Ansolysen), chlorisondamine (Ecolid) and mecamylamine (Inversine).

*(Continued on page 534)*

# Let ULTRASONICS Help You

*by F. Rose*, INDUSTRIAL CONSULTANT, TORONTO, ONTARIO

*The latest advances in simple mechanically-generated ultrasonics are helping cosmetics and pharmaceutical manufacturers with their homogenizing, emulsifying, dispersing and mixing problems, and produce better products faster and at less cost.*

Sound—whether it is within or outside our limited human range of hearing—is simply energy in wave form. It is the fast alternating motion of the particles of the medium through which it travels. We know of the difference of the speed of sound in air and in water and we know, through the popularity of high-fi music, that the frequency of these waves of energy normally heard by the average person is limited but, like eyesight, can be enlarged, sharpened or amplified by artificial means. Running a siren with increasing speed will cause a gradual increase of the frequency of sound until, at somewhere between 15,000 and 20,000 cycles per second, the human ear ceases to perceive it, and only instruments can tell what further changes in frequency are taking place. This is the point where sonics—the application of audible sound—ends, and where ultrasonics—the application of inaudible sound—begins.

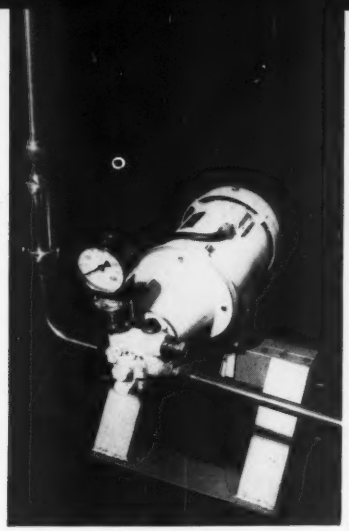
The audibility referred to is of course that of humans only. Certain animals, such as dogs, can hear higher frequencies, and special ultrasonic whistles, which are too high for our auditory senses to pick up, are perfectly audible to dogs and are used for training purposes. Bats can hear even higher frequencies up to 70,000 cycles per second, and use—in place of eyesight—the echo of their ultrasonic peeps, reflected from obstructions, as radar to prevent collision in pitch darkness. Ultrasonic waves can be produced either by piezoelectric, magnetostrictive or mechanical means, and it is the mechanical method which, because of its simplicity and low cost, has made such rapid progress in its application in the processing industries.

## Liquid Whistle

The mechanical generator of ultrasound, now available to industry, in a compact, easy-to-operate and inexpensive form, can best be described as a liquid whistle.

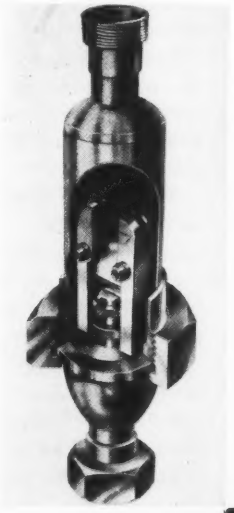
The ordinary toy whistle is an example of a sonic whistle. Imagine a similar device, only, instead of air, a liquid is blown into the whistle by a pump developing some 200 lbs. per square inch pressure and is allowed to rush over the sharp edge of a thin, easily flexing stainless steel blade, which is only partly supported, so that the sharp-edged side is able to vibrate in the liquid stream as it passes over and around it, in the same manner as the leaves of a book will begin to flutter or vibrate when air is blown edgewise against them, a principle known as the the vibrating reed, and used in the mouth-organ to produce audible sounds.

The liquid is made to emerge under pressure from a slit-shaped nozzle, in a flat jet, and the sharp-edged blade, on which the jet of liquid impinges, is so clamped, that it will vibrate at its own frequency, which is about 22,000 cycles per second, just a little above the upper audible limit which we can perceive with our sense of hearing. No detrimental



effects of any kind are caused by these frequencies to the operator, and the ultrasound produced is completely harmless.

When liquid is subjected to ultrasound, a phenomenon takes place which is known as cavitation. It is the rapid formation of cavities or tiny bubbles which are filled with the vapor of the liquid and which collapse continuously. This is sometimes referred to as "cold boiling" and causes temendous acceleration of the molecules, with resulting pressures of up to 30,000 lbs. per square inch, localized in the immediate vicinity of the vibrating blade. This action can be compared to a continuous series of minute explosions of great destructive impact intensity within the liquid, resulting in extensive hydraulic shear, causing particle size to be broken



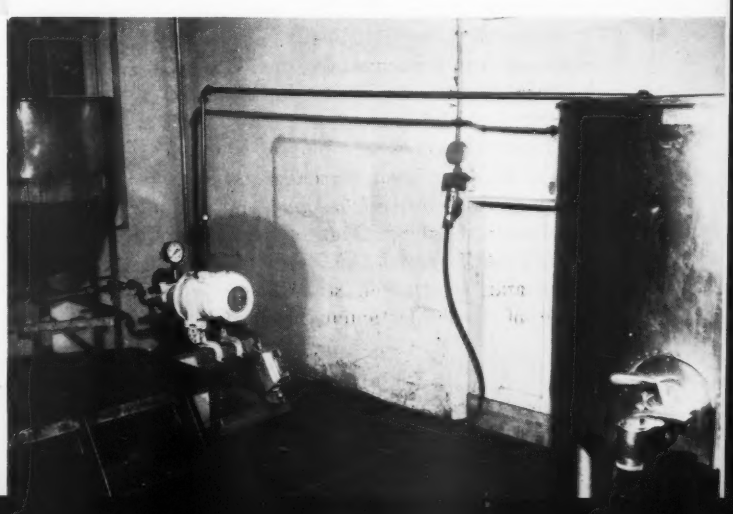
and finely divided down to one micron (40 millionth of an inch). This produces an intimate mix of immiscible liquids which would normally separate, i.e. it produces a stable emulsion of oil and water. It also causes agglomerates, or clumped clusters of particles, to be broken up, floating material to be wetted, reacting surfaces to be more intimately contacted, and solids to be finely dispersed in liquids, so that they stay in suspension instead of settling out. In processing industries, such as food, cosmetics, pharmaceuticals and other fluid chemicals, this effect is now being utilized for homogenizing, emulsifing, dispersing and intimate mixing, with considerable reduction in processing time and increase in product uniformity.

### 450 G.P.H. with 2 H.P. Motor

The outstanding advantage of this method is its simplicity and low cost. While the method is ultrasonic, the equipment includes no electronics, no intricate piping or wiring and no sensitive mechanism requiring special skills or training for operation and upkeep.

The standard production unit, which handles up to 450 gallons per hour (according to viscosity), comprises a 2 H.P. totally enclosed motor, driving a high speed positive displacement type gear pump which incorporates an overload relief valve and by-pass. For larger throughputs any required number of these units can be connected in parallel. For smaller throughputs a by-pass return system is normally used, or the Laboratory and Pilot Plant Unit which is referred to later. For abrasive or otherwise difficult liquids or slurries, slow speed gear pumps, or progressing cavity type pumps are available for both, production and laboratory size operations.

*(Continued on page 543)*



# Antibiotic Considerations in the

*by Wm. Burdell Baker* DIRECTOR OF FIELDS SALES, ANTIBIOTIC DIVISION, S. B. PENICK & CO., NEW YORK, N. Y.

**Table No. 1**
**PENICK ANTIBIOTICS IN PRODUCTS**
**Rx and Non-Rx**

| | Topical | Lozenge | Nasal | Ophthalmic | Human dysenteries, diarrheas, intestinal antisepsis, etc. | Cosmetic and Allied | Needs NDA | Needs To Be Certified |
|---|---|---|---|---|---|---|---|---|
| Neomycin | Non-Rx | To be Resolved | Non-Rx | Rx | *Rx | To be Resolved | Yes | No |
| Bacitracin | Non-Rx | Non-Rx | Non-Rx | Rx | *Rx | To be Resolved | No | Yes, except plain bac. ointment |
| Tyrothricin | Non-Rx | Non-Rx | Non-Rx | Rx | —— | Non-Rx usually | No and Yes | No |
| Gramicidin | Same as tyrothricin | | | | | | | |

Note: Above situations apply if other ingredients in products do not complicate. For example, topical ointment of neomycin-cortisone is Rx.
*In export field used in amebic dysentery, etc. Whether Rx or non-Rx would depend upon laws of individual countries.

In cosmetic products increasing emphasis is being placed on the contributions made by active agents that are parts of certain formulas. Active agents which influence the ability of the product to attain topical esthetic effects may be of particular value.

A certain small group of antibiotics could possibly qualify for such contributions of activity in cosmetics, particularly if dermatological improvement and subsequent enhancement of the skin appearance would result.

The considerations of antibiotics in the cosmetic and allied fields should be selective and should be scientifically evaluated. The reason for the need of selectivity is clear. It is because many antibiotics have relatively high incidences of allergic sensitivities and drug resistance. Penicillin, streptomycin and broad spectrum antibiotics are included in this category. Obviously such potent agents must be used, even topically, under proper medical guidance and consequently their usage is controlled by legally requiring their administration by a physician's prescription.

There are a few antibiotics which are virtually non-toxic when used topically, or even orally, and which have records of low incidences of allergic sensitivities and drug resistance. *TYROTHRICIN*, *BACITRACIN* and *NEOMYCIN* are in this category and, in general, share these properties. Because of these particular properties they are permissible for use in many drug products sold over-the-counter, without prescription, in drug stores.

Inasmuch as tyrothricin, bacitracin and neomycin are acceptable in many non-prescription products we can properly reason that there should be instances where they would be permissible in certain cosmetic allied products.

What potentials do these antibiotics have to offer in such products? This can best be determined by a study of their present behavior and uses, particularly as related to products for skin application.

Combinations of certain of these antibiotics are also feasible and may offer advantages. For instance,

Some micro-organisms do not respond to single drugs. To deal with variety of bacteria (mixed infections). Attain higher percentages of cures.

Economy (when synergism exists)

It should be explained that the three antibiotics discussed are either usable as such in products or are related to compounds, salts or extractives of which may be employed instead because of better practicability or some other advantage. The relationships are shown in Table No. 7.

Even though neomycin is frequently mentioned in the literature as the base it is most often used as neomycin sulfate in products. Bacitracin is employed as such or as its zinc salt; or as the compound, bacitracin methylene disalicylate. At this time

*Presentation, Society Cosmetic Chemists, Chicago Chapter, March 12, 1957.
†Developed by S. B. Penick & Company, Research Laboratories.

# Cosmetic and Allied Fields*

bacitracin methylene disalicylate is utilized in veterinary products and the purified form of this compound has much potential for human use. Tyrothricin is utilizable as such in certain products and more recently gramicidin, the antibiotic that represents essentially all of the activity of tyrothricin, is being used in products to an increasing extent.

While tyrothricin is a leading antibiotic possibility for usage in cosmetic products, neomycin is also worthy of evaluation because of several of its properties as follows: it has versatile action against gram-positive and gram-negative skin bacteria, it is nontoxic when employed topically (or orally) and has a very low incidence of sensitivities and drug resistance.

The sulfate of neomycin has been reported[1] as having successful deodorant action. The dermatologists reporting state that the repeated application of neomycin cream of lotion completely inhibited the production of odor in the axilla of 20 men. They also point out that this work provides further evidence that axillary odor results from the action of bacteria on apocrine sweat and that this deodorant treatment provides an alternative measure in those instances where the standard aluminum salt deodorants are not tolerated.

**Table No. 2**
**ANTIBIOTICS SPECTRA**

| Neomycin (Bactericidal) | Tyrothricin (Bacteriostatic) |
|---|---|
| 1. Strongest against gram-negative bacteria | 1. Gram-positive bacteria |
| 2. Many gram-positive bacteria | 2. A few gram-negative bacteria |
| 3. Most actinomycetes | 3. A few spirochetes |
| 4. A few yeasts | |
| **Bacitracin (Bactericidal)** | |
| 1. Gram-positive bacteria | |
| 2. A few gram-negative bacteria | |
| 3. A few spirochetes | |
| 4. A few protozoa | |

**Comments**

Neomycin: Note versatility because active against both gram-negative and gram-positive bacteria.
Bacitracin: Note strong action against gram-positive bacteria.
Tyrathricin: Note action against gram-positive bacteria.

**Table No. 3**
**TYROTHRICIN AND GRAMICIDIN USES**

Pharyngeal infections
Dermatological (pimples, acne)
Skin deodorant*
Potentials: soaps, cosmetics, shampoos, etc.

*Note: Deodorant market represents one of the largest cosmetic markets: creams, soaps, sprays. Tyrothricin is presently major potential in cosmetic and allied fields. Success of over-the-counter product acceptance would depend upon nature and kind of data collected.

**Table No. 4**
**NEOMYCIN USES**

Dermatological
Nasal, ophthalmic, aural, pharyngeal infections
Intestinal antisepsis
Diarrheas
Potentials: Cosmetic, Skin deodorant*, etc.

*Note: Neomycin potential in cosmetic and allied fields second only to tyrothricin.

**Table No. 5**
**BACITRACIN USES**

Dermatological
Ophthalmic, aural, nasal, pharyngeal infections
Amebic dysentery, etc.
Systemic by injection
Potential in cosmetic and allied field because of bactericidal gram-positive action against skin bacteria

Export Use: As purified bacitracin methylene disalicylate combined with chemical amebicide. Being thoroughly investigated as treatment for human amebiasis (amebic dysentery).

**Table No. 6**
**COMBINATIONS**

For additive, potentiating, synergistic, companion actions
Reasons for combinations: Human and veterinary

| | For *Synergistic Effects | For Other Effects, Above |
|---|---|---|
| Neomycin with | Bacitracin | Gramicidin |
| Bacitracin with | Neomycin<br>Tyrothricin | Tyrothricin |
| Tyrothricin with | Bacitracin | Neomycin |

*Refers to one antibiotic helping action of the other, and vice-versa. Synergism potential exists with many other antibiotics and chemicals.

Neomycin palmitate is a new salt which has been developed recently.† It is a whitish free-flowing powder with a smooth "silky" feel and a pleasantly clean odor. It is essentially insoluble in various

fixed oils as well as glycerin and propylene glycol, and soluble in ethyl alcohol to the extent of 1-3 per cent.

A comparison of the *in vitro* spectrum data between neomycin palmitate and neomycin sulfate is given in Table Nos. 8 and 9 respectively.

The reasoning behind the view that tyrothricin, bacitracin and neomycin should be permissible in ceratin cosmetic or allied products must be supported, of course, by satisfactory data. The implications for usage of these antibiotics would be determined primarily from established findings in the dermatological field. This is not difficult to do because of the abundantly available literature data pertaining to their skin applications.[2]

However, provisions of the Food, Drug and Cosmetic Act also must be met. Before marketing is permitted, one or two requirements are in order depending on which portion of the Act covers the product. Either (a) a "new drug application" must be submitted to the Food and Drug Administration or (b) "certification" must be obtained through the Division of Antibiotics, Food and Drug Administration.

It is realized that cosmetic firms have not often been concerned with the need for submitting "new drug applications". Many have never dealt with such procedures. However, with the increasing tendency to adapt therapeutic agents to use in cosmetic products there is a simultaneous need for becoming better acquainted with the "nda" procedure.

A "new drug application" is submitted pursuant to section 505 (b) of the Federal Food, Drug and Cosmetic Act. This section is concerned essentially with product safety. Whether a product is required to go through the "new drug" procedure primarily will depend upon the nature of the formula and the claims intended to be made. If it is a "new drug" within the meaning of the Act then the "new drug

*(Continued on page 552)*

**Table No. 7**

**ANTIBIOTICS MADE BY S. B. PENICK AND COMPANY**

1. Bacitracin, U.S.P. quality
   Compounds and Salts
   2. Bacitracin methylene disalicylate (DPS): veterinary grade source of bacitracin activity.
   3. Soluble DPS: vet. use.
   4. Purified DPS: potential human use.
   5. Zinc bacitracin: human or vet. use.
6. Neomycin sulfate, U.S.P. quality
   7. Neomycin sulfate, not U.S.P.
   New salts being evaluated: neomycin palmitate and others.
8. Tyrothricin
   Active Principles:
   9. Gramicidin: major
   10. Tyrocidin: minor
11. Candicidin: experimental fungicide, especially against monilia (candida albicans)

**Table No. 8**

Experimental In Vitro Spectrum Data Showing Neomycin Palmitrate as Active as Neomycin Sulfate. The minimal inhibitory concentration of the drug is recorded as the lowest concentration in mcg./ml. necessary to inhibit growth.

| Culture No. | Fungi | Neomycin Palmitate | Neomycin Sulfate |
|---|---|---|---|
| M63 | Candida albicans | 500 | 500 |
| M260 | Cryptococcus neoformans | 500 | 500 |
| M80 | Microsporum audouini | 15.6 | 125 |
| M82 | Microsporum gypseum | 15.6 | 500 |
| M161 | Sporotrichum schenckii | 62.5 | 500 |
| M302 | Trichophyton mentagrophytes | 31.2 | 250 |
| M303 | Trichophyton rubrum | 62.5 | 500 |
| M304 | Trichophyton tonsurans | 500 | 500 |
| M200 | Hormodendrum pedrosoi | 15.6 | 500 |
| M270 | Allescheria boydii | 62.5 | 500 |
| M83 | Microsporum canis | 31.2 | 500 |
| M408 | Torulopsis utilis | 62.5 | 500 |
| M414 | Rhizopus nigricans | 62.5 | 500 |

**Table No. 9**

Experimental In Vitro Spectrum Data Showing Neomycin Palmitate as Active as Neomycin Sulfate. The minimal inhibitory concentration of the drug is recorded as the lowest concentration in mcg./ml. necessary to inhibit growth.

| Culture No. | Bacteria | Neomycin Palmitate | Neomycin Sulfate |
|---|---|---|---|
| 100 | A. aerogenes | 1.56 | 3.12 |
| 311 | C. diphtheriae | 0.10 | 0.10 |
| 401 | S. typhosa | 3.12 | 12.5 |
| 536 | E. coli | 6.25 | 12.5 |
| 554 | H. influenzae | 25.0 | 6.25 |
| 558 | H. pertussis | 6.25 | 1.56 |
| 602 | K. pneumoniae | 1.56 | 3.12 |
| 720 | Pr. vulgaris | 25.0 | 6.25 |
| 813 | Pr. aeruginosa | 12.5 | 12.5 |
| 910 | S. schott (para B) | 6.25 | 25.0 |
| 959 | Sh. paradysenteriae | 25.0 | 12.5 |
| 1200A | M. pyogenes Var. albus | 0.78 | 0.78 |
| 1209 | M. pyogenes Var. aureus | 1.56 | 3.12 |
| 1206 | M. pyogenes Var. citreus | 3.12 | 6.25 |
| 1216 | M. pyogenes Var. epidermidis | 1.56 | 0.39 |
| 1300 | St. viridans | 3.12 | 100 |
| 1307-3 | St. hemolyticus | 0.78 | 6.25 |
| 1307-4 | St. pyogenes | 0.20 | 1.56 |
| 1341 | St. faecalis | 50 | 100 |
| 1900 | D. pneumoniae | 1.56 | 12.5 |
| 1054-3 | Cl. perfringens (ATCC) | 3.12 | 250 |

**Table No. 10**

**NEW DRUG APPLICATION. CERTIFICATION**

| Products Containing | (a) Needs "New Drug Application" (Agency: Food and Drug Administration) | (b) Needs to be "Certified" (Agency: Div. of Antibiotics, Food and Drug Administration) |
|---|---|---|
| Neomycin | Yes | No |
| Bacitracin | No | Yes, except Bacitracin Ointment |
| Tyrothricin | No and Yes | No |

# Packaging and Selling

An aerosol applicator specifically designed for a nasal spray has been introduced by Valve Corporation of America. Using the new metered valve which measures precisely the amount of each application, physicists at VCA have developed a simple two-piece dispenser, shaped for easy administering to the user's nostrils by pressure of the fingers that hold the spray. The controlled dispersion penetrates the blocked nasal channel and gives the full intended effect of the medication. The spray's dose can be delivered in amounts from 50 mg. Since each ejection is exactly the same, the number of treatments can be definitely stated on the label.

# OWENS-ILLINOIS ASSURES YOU A

**Co-ordinated Research**

*Pure research* into formulae and fabrication of glass, *packaging research* into processing and handling methods in customer plants, and *market research* into consumer attitudes, add up to greater specific value for your packaging dollar.

**Engineered Design**

The package that takes your product to market must take *three* needs into account. Considerations of its function in the retail store, its operating efficiency and its consumer utility all become a part of the prescription for an Owens-Illinois package.

**The Right Container**

Versatility of facilities enables Owens-Illinois to supply containers to meet special needs: Duraglas containers for almost any item; Libbey Safedge packing tumblers or premiums; Kimble Ampuls and Vials; and a variety of Owens-Illinois plastic containers.

# The right closure sells

# How to be a good salesman

*by Frazer V. Sinclair*

Are good salesmen born that way or are they trained that way? There is a hardy difference in the opinion of sales managers on this subject. Over the last year or two we have published several surveys and experiments by leading business colleges trying to find the anwser. The bulk of opinion seems to be that training carries more weight than birthright.

Whatever it may be that makes a good salesman click, everybody in selling knows that there are vast differences among salesmen. What we do not know and ought to know is how much of the blame for a salesman's failure to reach effectiveness should be placed upon the training and supervision by the company.

We do not like to bring military terms into a discussion of the function of selling, but they have been used in the past, and in some cases, they seem to precisely describe a particular problem. For instance, we could say that the planning and the staff work at company headquarters is the basis of the strategic operation for selling and that the salesman out in a territory is the tactician who is operating on his own but must conform to the general overall plan from headquarters. If the tactician falls down, or if he is not given an effective strategic plan, then obviously something must have gone sour.

There has been quite a bit of study lately, particularly by the daily newspapers, of the national distribution of quite a number of leading brands. It is startling to look at the distribution picture of these brands which are sold nationally and advertised nationally. In practically every case there are unexplainable peaks and dips, pluses and minuses. We say unexplainable because some of these exaggerated pluses or exaggerated minuses cannot be explained by social or geographical or economic conditions in any territory, nor by the inadequacy of the national advertising, nor, in fact, by any conditions except possibly the local inadequacy of the salesman or the local inadequacy of retail selling ability.

It is customary in business today to prepare large national advertising campaigns and as an adjunct of this advertising to carefully prepare point of sale material, promotions, and all the coordinated paraphernalia of a merchandising plan. It is then customary, in too many companies, to toss this at the salesman in an annual sales meeting and probably fail to follow up to see how he is using this material.

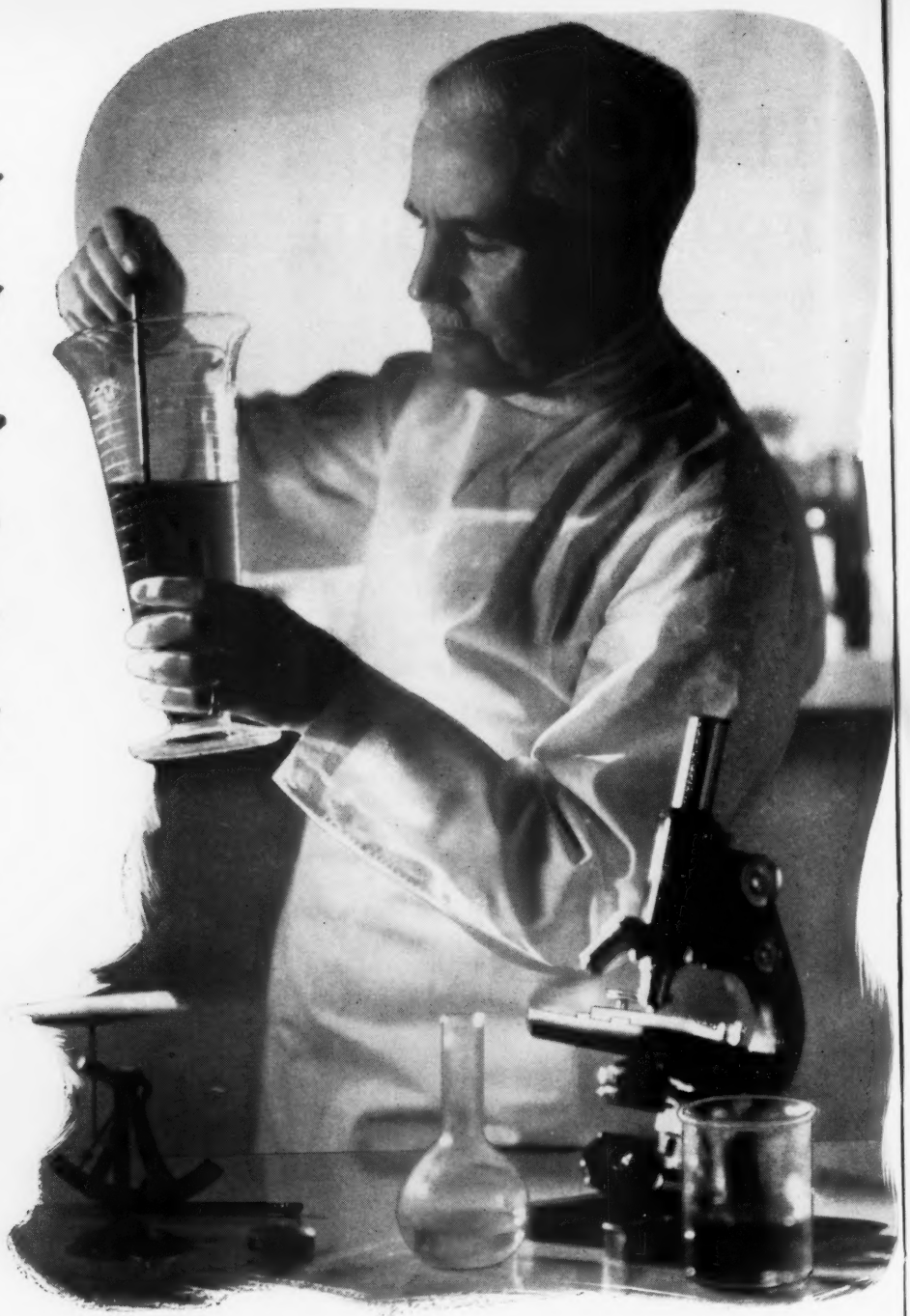
It is a fact that in many cases, perhaps today in a majority of cases, the salesman for a company which has been a long established national advertiser, hardly mentions this advertising to a retailer any more, practically never opens up his advertising portfolio, or discusses the company advertising with his customer. Advertising on both sides has become stale news. The result, very often, is that an unusually effective campaign by the advertiser or a substantial increase in spending is not properly relayed to the retailer.

A salesman may be a prima donna. He may have his territory in his pocket. He may be an opinionated individual, an egotist and a lot of other things, but even if he is a good producer, it is his duty to use every single sales tool which the company provides and it is a plain blunt necessity for the company to see that he does. Certainly, it would be ridiculous to think that a company should spend a great deal of time and a great deal of money and have at its disposal some excellent creative minds in making ready these sales tools and then have the salesman ignore them or become too darn lazy or too interested in social gossip with his customers to employ them.

We are indebted to the National Advertisers Edition of "Grey Matter" of the Grey Advertising Agency of 430 Park Avenue, New York 22, N. Y. for the following analysis of the two parts of every

# glass containers move more drug products

*Use* **Anchorglass®** *containers sealed with* Anchor® *caps*



## ...because they are chemically inert

GLASS containers are chemically clean and chemically stable. Because they are high in chemical durability they cannot change your products... the purity, strength and other qualities which characterize them are effectively protected until the contents are entirely used up. They do not rust or corrode. They prevent evaporation, leakage or moisture absorption. And they invite product inspection, afford a visual inventory, inspire confidence for your product quality. Move more of your drug products—pack them in Anchorglass Containers sealed with dependable Anchor Caps.

ANCHOR HOCKING

**GLASS CORPORATION**

*Lancaster, Ohio*

sale. We think this is so well thought out and can be employed to such excellent advantage in analyzing company sales policy and in discussing this whole problem with a sales force that we produce here the complete program of sales cooperation between the salesman and his company.

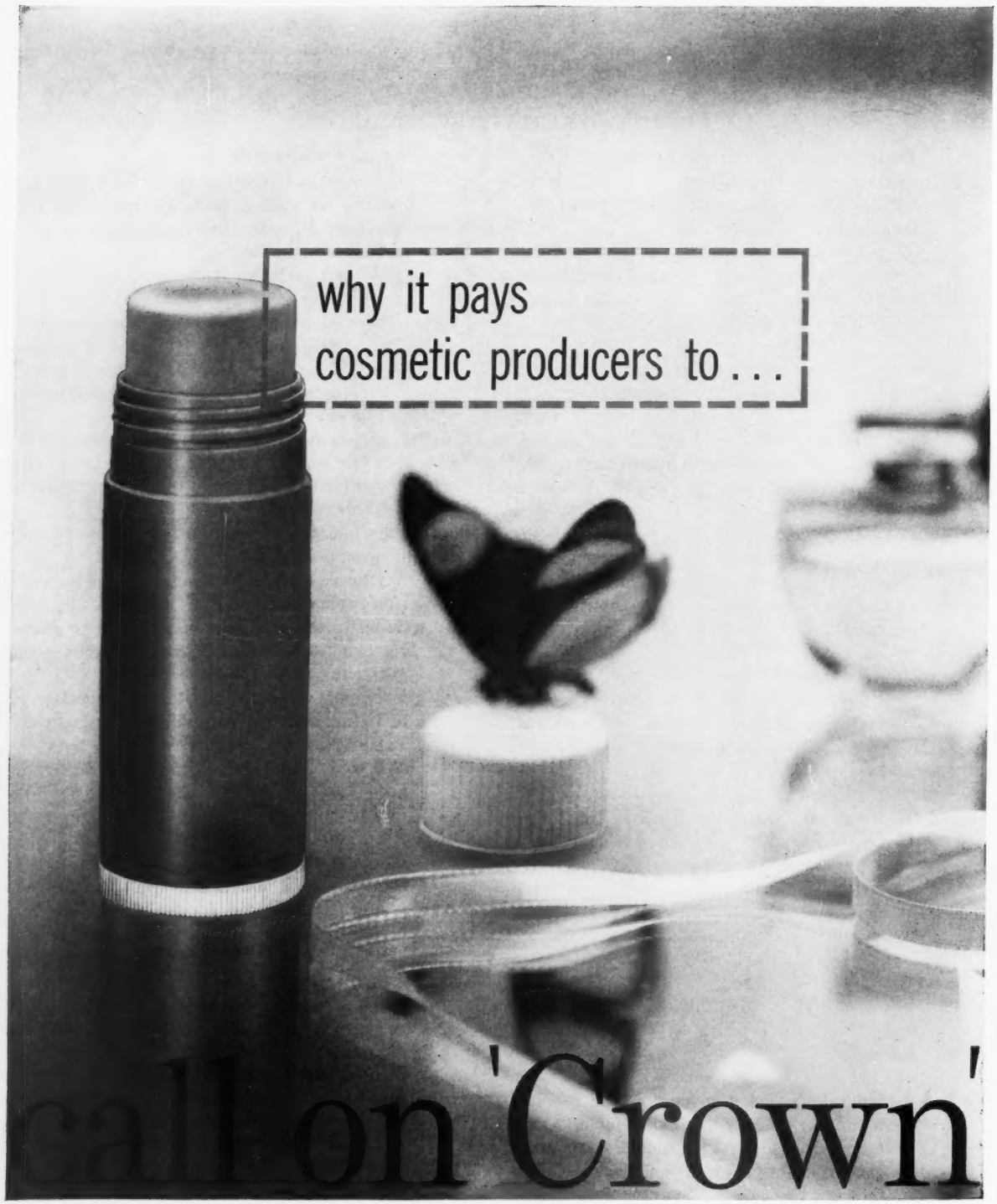
## THE TWO PARTS OF EVERY SALE

**The part which is done for you.**

1. Your company provides you with a product *skillfully designed* and *thoroughly tested* to stand up against competition.
2. Your product has been *packaged* so that it will attract the customer, and also fit in the retailer's shelf or floor plans.
3. Your product has been priced to *compare favorably* with competitive products.
4. Your outlets have been *carefully determined* to make your product available to the largest number of customers.
5. *Doors to the trade* have been opened for you by planned trade advertising and promotion. You never have to call "cold turkey" with an unknown product by an unknown company.
6. You are provided with *efficient selling tools.* Even your presentation has been thought out, blueprinted and put into graphic form to save you time and effort in telling your story.
7. Your sales or product manager is your *helpful guide and leader.* He keeps you constantly informed on new items, new lines, new uses for the product, new selling points, examples of successful promotions by dealers, threats by competition, opportunities for new accounts.
8. *Dramatic advertising* creates acceptance or desire for your product on the part of the consumer.
9. Added sales speed is given to your product from time to time by *merchandising* and *promotion* devices such as premiums, couponing, tie-ins, contests, dealers' and salespeople's incentives.
10. Since display is so vital in moving merchandise out of the store, your company provides point-of-sale material to *help the retailer sell.*
11. Your company has set up efficient re-order and delivery systems to *insure* that your customers have plenty of merchandise on the selling floor and in reserve at all times.

**The part which you do.**

1. Know *everything there is to know* about your product, its selling features, its points of superiority, its uses. Be *expert* in demonstrating it.
2. Know and understand the why and wherefore of your *product's packaging,* why it's superior in design, coloring, shape, function.
3. Start with a *sincere belief* in your product's value. If a cheaper price is the whole story, would there be a need for good salesmen . . . or any salesmen?
4. Your job is to *cover every single prospect* in your territory rather than deciding independently which type of outlet to solicit and which to ignore.
5. Use time thus saved for you to give your prospect *sound selling ideas.* A good idea may turn a reticent buyer into a rabid booster.
6. Don't shortchange your company by deciding to tell only part of the story or glossing over it. A good salesman, like a good workman, *uses his tools* efficiently.
7. Your part of the sale is to *take advantage* of this guidance and leadership enthusiastically and intelligently. Reciprocate, too, by keeping your leader informed about successful promotions in your territory and of competitive products.
8. Appreciate that your company's advertising is like a *modern machine.* It produces customers faster and cheaper. Show it. Dramatize it. *Make it work for you.*
9. What *you* do with these merchandising and sales-accelerating devices makes the difference. *You* hold the throttle. Their speed and their power to produce depend on *your* success in getting your customers to use them. Help your customers plan promotions. Be ready to suggest ideas for linking your products with related products to provide handles for department-wide or store-wide promotions.
10. Keep a sharp eye on *display opportunities.* Suggest ideas for using the material your company has created. Accept as a personal challenge any display preference given to competitive brands.
11. As the *sales promotions manager* of your company in your territory, be a "hound-dog" in flushing out thin stock and out-of-stock conditions; in fighting for shelf position; and in striving for those *extra sales* which will mean extra volume for your customers.

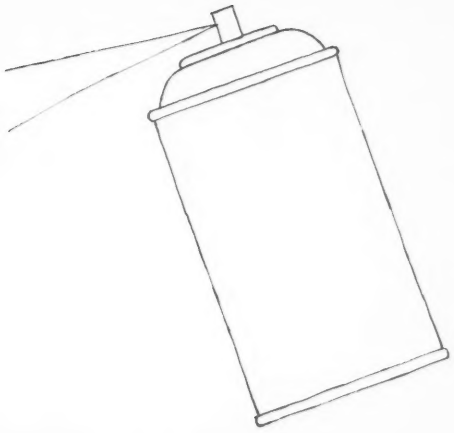



They want and *get* a new twist in packaging. Crown's plastic Seal-Stik, for example, is an eye-catching and easy-to-work container for colognes and deodorants. It closes tight to preserve product quality on the shelf as well as in pocket or purse. It is giving dozens of products extra sales advantages at the point-of-sale.

Crown's broad experience in packaging . . . in equipment for filling and closing glass, metal and plastic containers . . . combine to provide *packaging service* that pays real dividends when you . . . *call on Crown.*

CROWN CORK & SEAL COMPANY, INC., BALTIMORE 3, MARYLAND

# Aerosol Packaging



*by Frank W. Blodgett*
"FREON" PRODUCTS DIVISION
E. I. DUPONT DE NEMOURS & COMPANY

Six products account for nearly 90 per cent of the total aerosol market. These are the insecticides, the room deodorants, the hair sprays, the shave lathers, the Christmas snow, and the paints and lacquers. All of these products, and many of the other aerosol product types, require skillful perfuming for the best consumer acceptance.

Perfuming aerosol products requires a special skill. Even though an entirely satisfactory scent has been created for a nonaerosol product, with due regard to its compatibility with soap or other active ingredients, this scent may not be usable without some changes for the corresponding aerosol product. The entire scent is atomized with the product, rather than evaporating normally. This may give a false top note and a different residual odor.

On the credit side of the ledger, aerosol packaging protects essential oils from odor degradation by protecting the product from light and from atmospheric moisture and oxygen.

The "Freon" propellents are made under rigid quality control specifications. Since they have a very narrow boiling range, and contain very little residue (less than 0.05 per cent), they have only their faint characteristic odor, which we describe as "ethereal". This odor can usually be covered by the perfume formulation used. And since they contain no free acidity, and contain only minute traces of moisture (less than 5 parts per million), the propellents do not themselves cause any degradation of odor through chemical change.

The propellents have a very favorable inhalation toxicity rating in the Underwriters' Laboratories classes 5 and 6. They are entirely safe and suitable for use in personal and cosmetic aerosol products.

Aerosol products have a very good acceptance among consumers and retailers. One of our recent surveys showed that more than seven of every ten women who try aerosol colognes prefer them over nonaerosol colognes. Since only 26 per cent of the women interviewed had ever heard of aerosol colognes, there must be a large potential market for aerosol colognes.

*Abstracted from a talk delivered February 20, 1957 before the American Society of Perfumers.

As an example of the rapid growth of another cosmetic item, only two per cent of the women interviewed in 1951 used hair spray. By 1955, 50 per cent of the women told us that they used hair spray. There is obviously a very large market potential for well-formulated aerosol products which serve a real consumer need. And we have found that in many cases aerosol business is new business, in addition to sales of existing nonaerosol products.

But what limitations are there on aerosol packaging? We are trying to develop aerosol systems that will make it possible to spray almost any kind of liquid or powder, and to dispense other products as pastes or foams.

The newest aerosol system is the water-in-oil emulsion system developed by Dr. P. A. Sanders at the "Kinetic" Laboratory. This system is radically different from the previously used systems for dispensing water-based products. The most important water-based product, of course, is shave lather. This is an oil-in-water emulsion of propellent in the aqueous solution of soap and other ingredients. It is dispensed as a foam because the "propellent", being the internal or "oil" phase of the emulsion, blows bubbles in the soap solution when it expands as it is released from the valve. Oil-in-water emulsion systems tend to foam rather than spray.

Sprays can be made using the "three-phase" system, in which vapor from a shallow layer of propellent on the bottom of the container forces the main aqueous solution up through a dip tube (which is cut off just above the propellent layer) and out through a special atomizing valve. This system, unlike the regular homogeneous system, in which the "propellent" is dissolved in the solution of active ingredients, gives a coarse, wet spray, because practically none of the "propellent" vapor enters the valve to help atomize the aqueous solution.

The new water-in-oil emulsion system makes possible a fine spray of water-based products. The propellent surrounds the droplets of water solution. These droplets are present in the container, and

(*Continued on page 551*)

AEROSOL
Look what's been happening in aerosols!
millions of dollars
250
200
150
100
50
0
1951
1952
1953
1954
1955
1956
Interested?
Call GENERAL today!
Source: CSMA

# PACKAGING

## can start a tidal wave of sales *for you!*

You've seen it happen again and again. A familiar product . . . new packaging in aerosol form . . . and sales roll up powerfully with the force of a tidal wave! Or a new product makes its first appearance in aerosol containers and becomes an overnight success.

Perhaps *your* next big opportunity lies in aerosol packaging.

If your product can be sprayed, brushed on, dusted or daubed, it's a candidate for aerosols. As your first move, call General Chemical. We will help you develop a formulation with the right pressures and compatibilities for product and container without cost or obligation . . . and can direct you to capable contract fillers who will put up your product in aerosols for test marketing and handle full commercial production, too.

To arrange for a special presentation on aerosols and the fast-growing aerosol market, write or call "Genetron" Department, General Chemical Division, Allied Chemical & Dye Corporation, 40 Rector Street, New York 6, N. Y.

**genetron®**
**aerosol propellants**

*The Right Propellant for Every Aerosol Need!*

***Call on General for:***

Free fact-packed technical manuals, market information

A complete aerosol research and development laboratory

Data on many promising new types of aerosols

Field assistance with propellant storage, handling

**GENERAL CHEMICAL DIVISION** · Allied Chemical & Dye Corporation
**40 Rector Street, N. Y. 6, N. Y.**

# Wooing the Doctor Through Closed-Circuit TV

Several thousand physicians sat in front of giant television screens in hotel ballrooms of twenty-two Midwestern cities on April 10 watching the third in Pfizer-Roerig's current series of closed-circuit television productions for doctors. While the use of closed-circuit TV to reach busy physicians is not a new idea, Pfizer is experimenting with a novel use of the medium in that the programs are devoted to non-medical subjects.

The first program in this series grew out of Pfizer's wish to get physicians together and, of course, to meet professional service representatives form Pfizer-Roerig on completely non--business terms. One

Left to right: James A. O'Toole, manager of field sales promotion, Pfizer Laboratories; Senator Henry M. Jackson; Charles A. Kapp, Western regional sales manager, Pfizer Laboratories; Joseph L. Stremfel, assistant manager of field sales promotion, Pfizer Laboratories.

Physicians and their wives at The Shrine Auditorium in Los Angeles watching the origination of a Pfizer-Roerig program.

of Pfizer's advertising agencies, Paul Klemtner & Company, Inc. was consulted on producing the series of TV programs. Ed Rasp of the agency's MIC Division, organized in 1954 to produce and develop audio-visual programs for physicians, in turn consulted Lawrence E. Spivak, chosen because of his experience in producing NBC's award-winning program "Meet the Press."

James O'Toole, head of Pfizer's field sales promotion department, Mr. Spivak and Mr. Rasp proceeded to create the present series, based in part on some of the techniques of news presentation pioneered by "Meet the Press."

The initial Pfizer program called "Election 1956" presented Leonard Hall, Republican National Chairman, and Paul Butler, his Democratic Party counterpart. They faced a "Meet the Press" panel of newsmen which included Mrs. May Craig, Ned Brooks, Marquis Childs and Richard Wilson.

"Election 1956" was carried via closed-circuit TV to eleven cities, largely in the East and South. The program originated in Washington D. C. on October 24, just before the national elections.

It was an immediate success. Physicians in Washington, Philadelphia, Baltimore, Jacksonville, and other cities responded to the invitation and came to see the program. Pfizer representatives conducted on-the-spot interviews with physicians immediately after the program was over and found that the medical men were delighted with the Hall-Butler "debate." One of the advertising publications later noted that nearly 80 per cent of the physicians invited attended the closed-circuit program.

Encouraged by the success of the trial program, Pfizer then scheduled two additional closed-circuits, to take in the West Coast and Mountain States, as well as the Central States. The second program "Is Revolution in the U.S.S.R. Possible or Impossible?" featured General J. Lawton Collins, (Retired), Senator Henry M. Jackson, and two former communist secret police members on a panel of experts on international affairs. Mr. Spivak arranged for the newsmen to include Mrs. Craig, Ned Brooks, Eugene Lyons, and Louis Fischer, all authorities on the communist state.

Produced in Los Angeles on March 20, over a network of sixteen cities the program was telecast from a special studio set up on the stage of the massive Shrine Auditorum. The Los Angeles Times in a

*(Continued on page 553)*

# Packaging and Selling

## Orchids for Beauty

One of the most beneficent uses to which this department can be put is to record some of the great historical events of this industry so that the facts of these events may be available for the future archives of the industry.

Several months ago we reported in this column a rumor that a European chemist had discovered in the pollen of the orchid some chemicals of such startling cosmetic value that the famous royal jelly of the bee might become obsolete almost before it had become intrenched in cosmetic usage.

Now we are able to report that this new cosmetic, scientific development is no longer a secret. Publicity has already reached this office and we understand that the cosmetics containing this remarkable substance are now on sale in a select few of the leading toiletry departments in the great fashion department stores. Rather than comment upon this astonishing research and development, ourselves, we are going to quote profusely from this publicity for the record and for future historians in the industry.

"Deep within the heart of the orchid—known to be the longest-blooming flower in all the world—is a precious pollen, recently discovered by French scientists to yield more beauty-building elements than any other vegetable substance ever known!"

"First to see the astonishing beauty-benefits in this potent colorless pollen was Orlane, who in 1953 in their famous French research laboratories, began development of the incomparable Orlane *Symphonie au Pollen d' Orchidee*. . . .six wondrous make-ups and treatments each compounded with the pollen designed to extend its enriching effects 24 hours a day!"

According to this company, the first exploratory investigations into pollen, begun in 1953 in Paris, came about as a result of Orlane's work on royal jelly with the late Professeur Leonard Bordas," beloved science-laureate of the Institute and the Faculty of Medicine of Paris, and the honorary Zoology Professeur of Sciences in Rennes."

According to a statement by this company, "Professeur Bordas, who devoted so many of his 92 years to the study of royal jelly, was well qualified to guide the research of the Orlane technical staff. And in a letter of December 1953 to Orlane's technical director, Egmont Desperrois, Bordas disclosed the intriguing discovery, *that the unusual power of the Gelee Royale was actually due to the radio-bacterium contained in certain pollens* which were absorbed by the bees and accumulated in their pharyngitic glands. "The letter further stated that this pollen was so exceptionally rich in proteins, pantothenic acids, amazing amino acids, thiamin, riboflavin, niacin, and other elements as to make it greatly beneficial for "corrective dermatology". "Why", said the Professeur, "wouldn't you make a beauty cream or maquillage with the orchid pollen extract as a base?" It was upon Professeur Bordas' learned recommendations that Orlane first began their research in 1953."

"When the initial investigations were conducted, Orlane chemists studied the usual sources of pollen-fruit trees, rock roses, heather and chestnut trees. However, their pollen proved to be too deeply tinted for cosmetic use, and so the Orlane researchers were drawn to look elsewhere. They were instantly intrigued by the Orchid. . .for not only was it almost colorless, but it was rich in all the beautifying elements, and in addition was exquisitely light and delicate in texture—perfect for cosmetic compounding."

According to Orlane research, "each year a woman's skin loses some of its self-rejuvenating powers. . . her cells are slower to build fresh, firm skin. Pollen of orchid is found to be bountifully endowed with all these need elements."

Undoubtedly, we will hear more of orchid pollen. Right now the research has been confined to the Brassocattleya species which is repeatedly referred to as "the goddess of all beauty orchids". But as in the case of Royale Gelee, once the inquiring minds of the industry are bent in this new direction we may expect some further amazing discoveries of the kind which has given this industry, in research circles, a reputation for imaginative thinking.

## Why is This?

The 16th Annual Beauty Reader Forum, which has just been prepared by the Fawcett Publications, poses a problem and a discrepency which we wish somebody would explain to us.

The Fawcett Publications cover an active and a substantial group of cosmetic consumers. As a matter of fact, we would say that such publications as True Confessions and Motion Picture come very

Microscopic examination for structure of plastic components after exposure to aerosol formulation

**IMITATED...BUT NEVER DUPLICATED–**

**THE** *Precision Valve*

From planning to commercial production, a new aerosol product requires infinite knowledge, effort and research. Almost every phase of human endeavor contributes its share to the completed product.

The final use, however, is dependent upon the proper valve, which is carefully designed, engineered, and manufactured to produce the proper dispersion of spray, mist or foam.

We at Precision are ready to help you, whether it be formula, package design, or production. Our facilities can be our contribution to the success of your business.

Whether it be a million and ten **or just ten**... Precision has or will develop the aerosol valve for your product. Our large quality control department assures you of the finest results along with the economy required for profitable sales.

*Known throughout the World*

PRECISION

*Precision Valve Corporation*

700 NEPPERHAN AVENUE • YONKERS 3, NEW YORK

near to representing the age group in the social strata in American womanhood that is at the peak of cosmetic usage.

This new survey gives the percentage use of the various cosmetics over the last ten years beginning with 1946. What startles us is that in the view of the enormous increase in the dollar sales of the cosmetic industry over this period of years that there is indicated here among primary cosmetic users so substantial a decline in cosmetic use covering so many different cosmetics.

For instance, here are the percentage use of leading cosmetics for the year 1946 and for the year 1956.

| | 1946 | 1956 |
|---|---|---|
| Anti-Perspirant and Deodorant | 96% | 95% |
| Bath and Talcum Powder | 80% | 72% |
| Bath Salts and Water Softeners | 29% | 14% |
| Cologne and Toilet Water | 81% | 65% |
| Cream for Cleansing | 68% | 44% |
| Cream for Powder Base | 37% | 23% |
| Cream for Softening or Lubricating | 51% | 27% |
| Eyebrow Pencil | 35% | 54% |
| Eye Shadow | 12% | 19% |
| Face Powder | 91% | 79% |
| Hair Rinses | 29% | 57% |
| Hand Cream | 46% | 37% |
| Hand Lotion | 78% | 80% |
| Lipstick | 99% | 99% |
| Nail Polish | 94% | 76% |
| Perfume | 69% | 48% |
| Rouge | 67% | 55% |
| Sachet | 31% | 24% |
| Shampoo | 96% | 97% |

### Chance for Small Business

Leading newspapers have spent a great deal of money and research to show how very few truly national distributed brands there are in this country. In spite of the enormous and growing volume of national advertising, these leading newspapers have established a tremendous basis of research material to prove that the established national brands do not seem to deter local and regional manufacturers from going after a share of the market.

While these surveys are primarily directed toward the advertising story of the newspaper, that is for nearly everybody advertising is a local problem rather than a national one, the surveys are particularly valuable in indicating the countless opportunities for small businesses providing they are content to stay small and to take every advantage possible which arises from a limited operation.

In a recent survey by the Scripps-Howard Newspapers in fifteen cities here's what was discovered about national distribution in basic food products.

Out of 190 brands of baked beans, only four are available nationally.

Out of 768 brands of frozen foods, four have national distribution.

In canned soup, there are only three nationally distributed brands out of a total of 143.

Canned salmon has 308 brands with one nationally.

Coffee has 337 brands in these cities, but only four nationally. And so it goes.

### Private Label Cosmetics

Most of the large grocery chains have their own private label merchandise and, in fact, in some of the basic categories of food, such as coffee, bread, orange juice, and some other staples, the private label sales in many chains far exceed the sales of any national brand.

It must have been understood that if cosmetics ever attained a point of real volume and profit in the supermarkets that we would find the private label brand popping up in this department of one or more of the chains.

Now we read that the A&P, which is plunging head long into the non-food program, is promoting its private label tooth paste Denti-Kiss. In this introduction, the store offers two tubes of paste and one tooth brush for 49 cents.

At the present time, the A&P tooth paste appears to be confined to the southern territory.

### Opinions Differ

Just as an example indicating that the leading retailers are not sure just where they want to go and what kind of stores they will eventually arrive at, take a look at the diverse polices between the A&P and National Tea.

After holding out for quite a number of years, the A&P made one of the most abrupt face-abouts in the history of retail merchandising, last spring. This enormous chain had rigidly adhered to its policy of food merchandising, scorning the non-food extravagances of many other chains and also scorning the palatial emporiums of some of their competitors. Up to this time the philosophy of the A&P was to retail food in the shortest line possible and the least cost for distribution. Now all of a sudden the A&P has jumped into non-foods and is experimenting with blankets, stuffed pandas, imported china, toys, table lamps, and an assortment and selection of merchandising that if brought together would challenge Macy's basement.

At just about this time the general merchandising vice-president of National Tea states, "The non-foods business for supermarkets is greatly overrated, and we, for one, feel there is so much to do in expanding our food business that we are not much interested in all the talk about non-foods."

National Tea sees only two non-food departments as permanent sections in its stores: health and beauty aids (about 200 items) and housewares (a limited selection) with rack jobbers preferred for both.

### Never Failing Sales Pitch

If there is any one thing in which Americans can lick the world, it is in finding a sales pitch, regardless.

Newspaper readers will remember the testimony of the heads of the big automobile companies in Washington hearings, where they demonstrated very earnestly that in this traffic crowded country with its restricted speed limits, that the trend toward excessive engine power was really a margin of safety.

The one that really pleases us, however, is the new line of the billboard companies. These people are now in an aggressive national combat to take

# Presenting the NEW exquisite

with the new FUTURA CAP, shown in black—also comes in brilliant GOLD-COTE... bright touches of elegance for the purse or boudoir.

RICHFORD SPILLPROOF* PERFUME FLACONS

*TRADEMARK

Observe the beautifully angled silhouettes of these EXQUISITE new perfume bottles, and note the perfectly blending FUTURA caps. When you consider that each is fitted with the fabulous SPILLPROOF feature, you can understand why we are so enthusiastic about them.

in 1 dram, ½ ounce, 1 ounce, and 2 ounce sizes

*Write now for samples and prices.*

Spillproof perfume bottles are the magic perfume containers that have launched millions of sales slips — their customer appeal and proved acceptance will help the sales of your product.

RICHFORD CORPORATION

OFFICE & PLANT: 3618 OCEANSIDE RD., OCEANSIDE, N. Y.
SHOW ROOMS: 350 FIFTH AVE., NEW YORK

over the new net work of national highways soon to be built with the tax payer's money.

The mere fact that the billboard people have the automobile clubs, most of the civic associations and most of the people against the idea of having our highways a continuous stream of gaudy billboards, does not bother the billboard sales experts of this new campaign in the slightest.

The billboard people have brought the psychiatrists to their rescue with a phrase "Highway Hypnosis" to describe the lulling effects of the scenery and such things as nature, on the normal driver.

A psychologist from Iowa State College has just testified, "Gaudy billboards are life savers. They keep the driver from going to sleep at the wheel." Oh Boy!

### Big Small Business

The cosmetic industry, in the higher brackets of prestige products, that is the perfume and some of the treatment lines, are well aware that a substantial, profitable business can be developed with a ridiculously small clientele of consumers and, we may add, as a sideline, with a ridiculously small number of retail stores.

It takes some very simple arithmetic to figure that a perfume company can do a $2 million business which should net at least $250,000 with not much over 200,000 people stepping up to the retail store to buy their product, in any one year. There are many companies in the cosmetic industry with an annual sales of from $500,000 to $2 million or $3 million a year whose names are known to less than 500,000 consumers and whose total consumer clientele, that is the people who actually purchase their product at retail, would run from one hundred to two or three hundred thousand people. This is out of a population nearly 170,000,000 people with over 60,000,000 women of the age to use cosmetics.

According to the Bride's Institute, 1,550,000 brides established new homes last year.

We would say that if anybody comes up with an idea that has a specific appeal to brides and which gives a particularly favorable talking point to this part of the population, that only one-quarter, one-third or one-half of this small segment of our population could establish a thoroughly substantial business.

And just to make it so much more easy, there is nothing a retailer loves so much as a promotion which attracts a particular kind of customer with money to spend elsewhere.

### Questions on Vending

While retailing by vending machines has been growing at a substantial pace, it nevertheless seems that there are specific limitations to this method of retailing. Several years ago a leading department store experimented with a large battery of vending machines in a leading bus station. The products displayed in these machines were popular convenience items. After several months this experiment was closed out.

A few months ago we reported that one of the leading supermarkets was arranging a battery of vending machines across the entire front of a new store then being built. These machines were to provide 24-hour service on basic food essentials.

Now we hear that the A&P is discontinuing its bank of outdoor vending machines at its Levittown, N. Y. supermarket. A report from A&P headquarters is, "Vending does not fit in with the operation at this time."

Another reported reason is that outdoor vending machines were cutting down on A&P store traffic.

### Abdicating Retailers

Some time ago we ventured the opinion that a great many retailers, particularly those who are using self-service selling, were on the point of completely abdicating the retailers' place in distribution as part of the selling chain. We ventured the opinion here that these abdicating retailers were turning all of the selling functions over to the manufacturer and, therefore, should be willing to accept the consequences. Some of these consequences, we believe, should be a willingness to accept a much lower operating discount for the limited service they were rendering, a greater willingness to accept blindly manufacturer's promotions, manufacturer's local advertising without change and an increasing willingness to accept the status of the human vending machine.

In a recent talk before an advertising club a Mr. Von Der Ahe, a vice-president of Von's Grocery Chain around Los Angeles, made this remark: "Supermarkets do not sell merchandise. That is the job of manufacturers, food processors and advertising agencies. Supermarkets sell self-service, and, for that reason, demand and acceptance for products must be established before the customer enters the selling area."

### Expanding Cosmetic Companies

According to a report from Willard Gidwitz, president of Helene Curtis Industries, Inc., the company plans to diversify its operations by producing proprietary drugs and acquiring a company in the ethical pharmaceutical field. This company's cosmetic sales are expected to rise about 30% this year to a record of around $55 million.

We have already reported Revelon, Factor and Shulton with similar plans for expansion into drugs.

### That Buying Mood

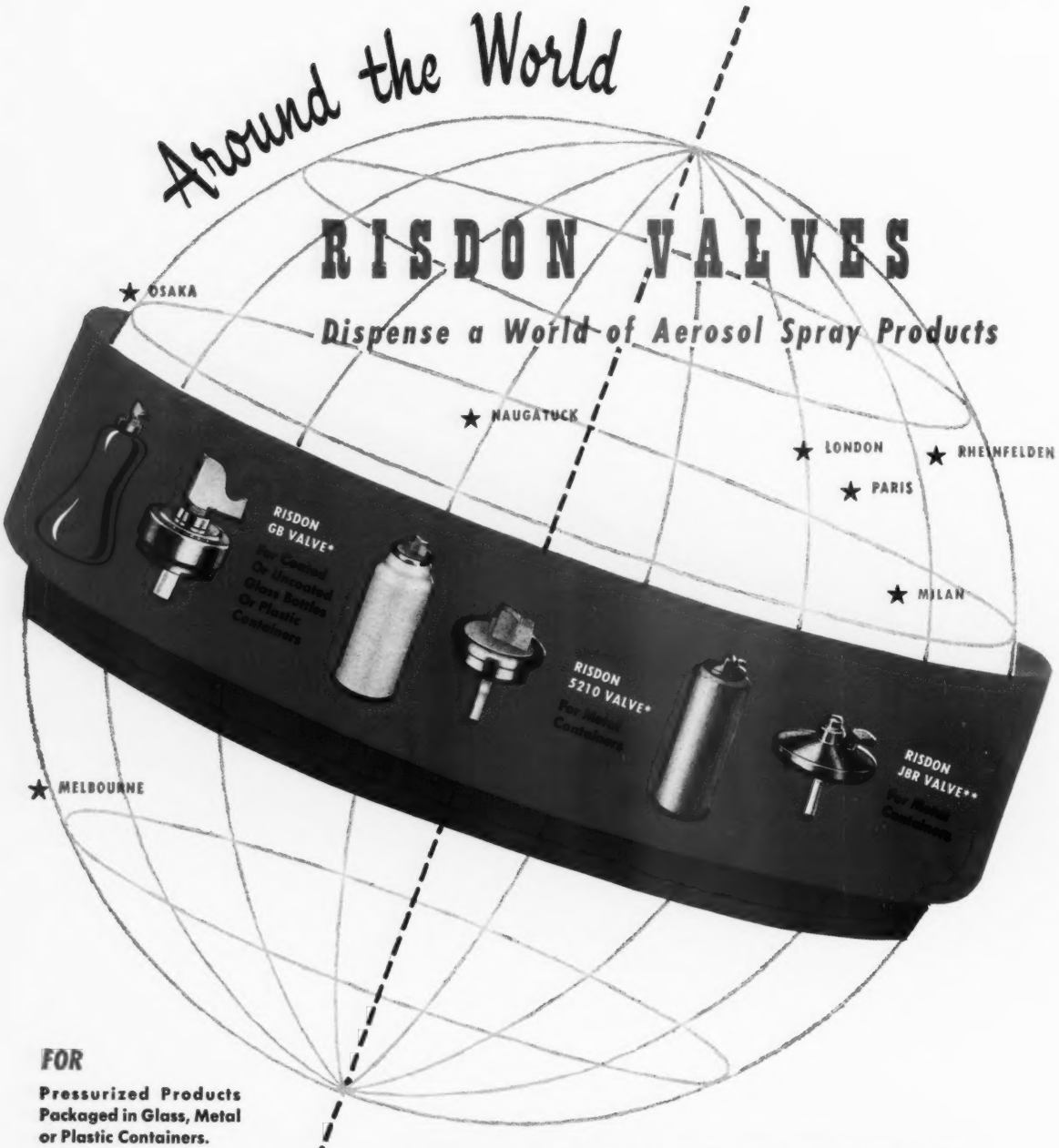
We have been intrigued recently in reading the new book "Selling the Supermarkets for Non-Food Manufacturers," to run across a few statements that do not at all meet with our way of thinking. For instance, to quote one sentence, "Customers in the supermarket are in a buying mood." And following this, "As a result, most women buy more than they plan to purchase on each visit to the supermarket."

We are perfectly willing to admit that customers go into the supermarket in a buying mood. Obviously. They are in there on a once or twice a week chore to buy the family groceries. While the suburban super-

# Around the World

# RISDON VALVES

## Dispense a World of Aerosol Spray Products




**FOR**

**Pressurized Products Packaged in Glass, Metal or Plastic Containers.**

**DISPENSING**

**Conventional Aerosols, 3-Phase Products, Alcohol Base Products, Water-Base Products, Foam Products, Powder Sprays, Metered Sprays, Ultra-Low Pressure Applications, Products Containing Propellent Emulsions or Dispersions, etc.**

* *Patents Applied For*
** *Patented*

Both geographically and in range of application, the Risdon line of aerosol valves covers a world of spray products.

They are produced by Risdon in the U. S. and by licensees* in England, Germany, Australia, France, Italy and Japan. Here and abroad, they enhance both the performance and appearance of metal, glass and plastic containers, dispensing a vast variety of product formulations.

*Write, today, for free booklets on any or all of the Risdon valves shown here.*

**THE RISDON MANUFACTURING COMPANY**
***Valve Division, Naugatuck, Conn.***

* GLENHAM PRODUCTS LTD., QUADREX HOUSE, PARK LANE, LONDON W1
PLASVERRE, 13-15 RUE TAITBOUT, PARIS 9
NATIONAL RADIATORS LTD., P. O. BOX 14, PORT MELBOURNE
AEROSOL INDUSTRIES CORP., FUJITA BLDG., OSAKA
SOLFRENE, VIA G. MATTEOTTI 12, CORSICO, MILAN
SPRÜHTECHNIK, RHEINFELDEN/BADEN, GERMANY

RISDON

market partakes something of a social center and to many a male who drifts in tagging behind his wife, it is a fascinating museum of packaged rarities, we say again that we agree thoroughly that the customers in the supermarket are there to buy.

We also agree, that in this rich and luxurious era the effect of impulse buying very often makes women purchase more than they expected to buy on many visits to the supermarket.

What we object to is the inference that since women enter the supermarket in a buying mood, they have money to toss around and are easy game for all sorts of non-food products.

We think that one of the troubles in the supermarket as an outlet for non-food products will some day be exactly the reverse of this mood. Right at this time there is a constant feeling of alarm at the mounting cost of the food basket on each visit to the supermarket. Under conditions of a less favorable economy, this fear could increase and have a drastic effect, not only on impulse buying, but on non-food products. We think there is a definite possibility that the women instead of going into a supermarket in a buying mood, with the inference of this statement, that instead many may go to the supermarket with a grim determination to hold down the cost of the food basket, not only to necessary foods, but even to the exclusion of a lot of pleasant impulses.

### Sellorama

The S. S. Kresge Company has created a new word in merchandising, at least so far as we know. This word is "Sellorama." According to the company, the word "Sellorama" means "raising the selling horizon" because "Orama" is the Greek word for horizon.

This new word is the campaign slogan for a very interesting trading up campaign for this chain during the coming year. Sellorama is a tour that will stop for three days at leading hotels in a number of cities where 750 different items will be displayed with models, skits, special displays, projectors, screens, and sound effects for a total of approximately 800 managers and superintendents.

### Point of Profit

It is refreshing to us to read that one of the major national advertisers and the owners of one of America's most famous brands, that is Coca-Cola, plans to make the point of sale a major part of their activity for the year. We say it is refreshing to read this because it seems to us that in this trade and particularly in the cosmetic business, that there have been a number of companies who have been going in just the opposite direction. Some of these cosmetic companies have experienced for the first time the expenditure of large sums for advertising. In some cases, these big expenditures have gone into television. These companies have reached such a stage of ecstacy in their new found power that they have taken the mental attitude that their big advertising expenditures to the consumer enables them to hold the retailer in contempt. These folks implicitly believed in those almost discarded phrases "consumer franchise," "consumer demand," or even "consumer acceptance."

Felix Coste, marketing director of Coca-Cola, in a recent speech called POP the "number one ad medium" and he said that his company's faith in point of purchase merchandising will run to the tune of about one third of this year's $15 million ad budget.

Mr. Coste defines POP as a point-of-profit and states there are three problems to be overcome: (1) getting good material; (2) getting it to the field; and (3) getting and keeping that material in a selling position.

As a further word of advice this executive states, "In our experience, the retailer is more susceptible to material that provides a service over and above selling our product alone. For one thing, he is more interested in campaigns that sell related products."

### How to Mark a Shipping Case

Here are some rules for marking a shipping case that seemed to us could be applied with great value in this industry. They were compiled by Ralph Johnson, executive vice-president of the National American Wholesale Grocers Association. These recommendations were adopted unanimously by the Inter-Industry Food Packaging Committee.

Markings on cases should be on all four sides.

Markings should be in bold print for easy reading.

When a manufacturer carries a broad product line, it would be helpful if product groups were differentiated by different type colors.

Where there are multiple lines, identification would be useful on the top and bottom of cases for more efficiency in unloading cars.

Lettering should not be less than one inch in height.

Print of the markings should leave sufficient space for retail selling prices on the outside of the case.

Identifications which are a must on the case are quantity, package or can sizes, brand name, and product name and variety.

Wherever any special unpacking problems are present, case opening instructions should appear.

If knives have to be used in opening the carton, the print should not be in a place where it will be obliterated when the case is cut open.

### Company Philosophy

An official at Pillsbury Mills, Inc. recently remarked at the meeting of the American Management Association that salesmen should be trained to understand more of their employer's philosophy, principles and methods.

He further stated that a deeper indoctrination of company philosophy in the sales force was one of the most important of the new patterns for marketing management.

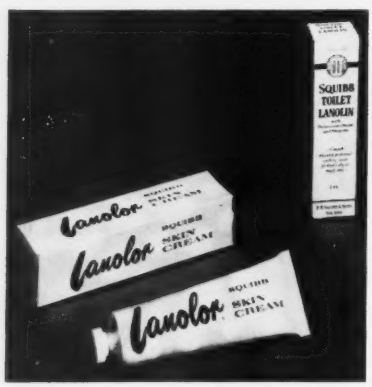
We, ourselves, are thoroughly in accord with this statement. We continually see salesmen working at cross purposes with what might be called the company philosophy or developing on their own something that they think that the company philosophy should be. The only trouble with this principle, which we again say should be essential not only in good selling but in developing a respected company personality, is that we wonder how many companies have anything called a philosophy.

# NEWS IN PACKAGING...

### Beauty-Fashion Promotion Aiding Squibb's "Lanolor"

Studies of consumer buying habits and uses for E. R. Squibb & Sons' Lanolor have prompted the company to utilize a beauty-fashion promotion for the product. Back of this tactic was a combined market research, advertising, and package design-promotion program, developed with Squibb by New York package and industrial design consultants Alan Berni & Associates.

Sales results in first month of market introduction, according to reporting stores and relayed by Squibb's merchandising products sales manager,

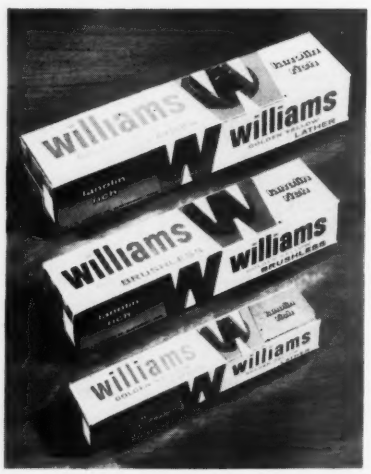



C. W. Lemkau "are triple and even quadruple sales for the same period last year with the old package and promotion."

Findings showed that while the product was touted primarily as a soothing, pharmaceutical lotion, women actually use it as a powder base and beauty cream.

Result: a switch in copy pitch,

French Frosting, a cosmetic foundation base made by Avon Products, Inc., comes in an unusually shaped jar made by the Hazel-Atlas Glass Division. The flat, one-ounce jar was designed to fit in with the decorative schemes of today's home boudoirs and vanity tables.




New shaving cream cartons featuring four-color printing over metallic foil have been engineered and produced by Container Corporation of America for the J. B. Williams Company. The new cartons make effective use of gold to stress the color of the cream itself, "Golden Yellow."

design and promotion – new jars, tubes, cartons and shippers, that double as displays in-the-store.

### Conn. Chem. Appoints Rader

Charles O. Rader has been appointed sales manager of the Contract Packaging Division of Connecticut Chemical Research Corporation, according to

CHARLES O. RADER

an announcement by A. O. Samuels, president.

Active in the product development, marketing and sales of a wide diversity of products, Mr. Rader has been supervisor of the Drug Division of Lever Brothers and sales promotion manager of the Tar Products and Chemical Division of Koppers Company, Inc., where he supervised the contract packaging section.

### Toni Deodorant Applicator

Hush, a new cream deodorant described as giving "deep cream protection without messy fingers," has been introduced by The Toni Company. The plastic case swivels up to measure out the amount needed and an applicator top spreads the cream and smooths it in. Hush will not dry out or harden because it is never fully exposed to the air, the company says.

"Extensive market testing of the product indicates that Hush meets all the requirements of the 'ideal' deodorant," said Stuart K. Hensley, executive vice-president of Toni. "The cream applies easily, dries quickly and provides complete protection. It is harmless to sensitive skin and delicate fabrics."

### Designer in Ciba Adv. Div.

Philip Swift has been appointed designer in the advertising division of Ciba Pharmaceutical Products Inc.

A plastic snap-cap intended for leak-proof sealing of collapsible tubes is available from J. Mart Co., 9015 Wilshire Boulevard, Beverly Hills, Calif. Consisting of two halves, the snap-cap's lower portion contains the dispensing nozzle which permanently fits onto the tube, while the upper half is connected to it by a plastic hinge. This hinging connection allows the top of the snap-cap to be flipped off easily and yet remain attached to the cap. Slight pressure of the upper portion against the lower snaps the overlapping ridges and grooves together to provide an effective seal.

# Patent thoughts and trends

*by Thomas Cifelli, Jr.*, PATENT ATTORNEY*

## IS NEW USE OF OLD MATERIAL PATENTABLE?

While this question is by no means a new one, it having been discussed in these columns from time to time over the years, contact with technical people demonstrates that there still is considerable misunderstanding on the part of many with regard to this question.

It is unfortunate that there exists so much misunderstanding because the question involves a field of invention which is very important, first, from the dollars and cents standpoint and, second, because the patent considerations are really extremely simple.

The economic aspect of this question is easily seen to be very important. For here, one is not dealing with mere new chemical compounds which have no known usefulness and which may never pass beyond the laboratory curiosity stage. No, here we are dealing with bread and butter solutions to practical problems. For example, let us assume that a company has, after considerable market research, determined that a cosmetic or drug preparation having certain properties and salable at a certain figure will have a wide market. The technical people solve the problem by combining a number of ingredients that have been known. The sales people are all set to go, advertising budgets, etc. are being considered, when someone raises the question of patent protection. Obviously, the question of patent protection is extremely important because upon the answer to this question may well depend the entire advertising and sales campaigns, if any, to be waged.

It really would be shocking, the the writer believes, if the truth were known as regards the number of times that someone in management has at this stage interjected a comment to the effect that he heard a talk or read an item which says that new uses of old materials are not patentable. There is no need to elaborate as regards the consequences of such a comment on the fate of the program under consideration.

Let us take a close look at the actual situation.

There are just 2 things that should be kept in mind at this point:

1. Forget about time-encrusted statements like "new use for old materials." In this connection, the patent field is not the only one in which there is considerable confusion simply because people just like to repeat words and statements that they have heard without really inquiring into whether the statements mean anything, or if they do, exactly what the statements mean.

2. Just remember that in the field of drugs and cosmetics there are two areas open to patent protection: 1. involves processees and 2. involves products or compositions. Forget the concept of covering a *use* whether new or old, as that is believed to be the source of most misunderstandings in this matter. While the patent law does require that a product or composition should be useful, among other things, before it is patentable, *U.S. patent law does not recognize the granting of patents on uses.*

Having reached this point, all that we need do is to ask ourselves whether there is something novel in the process or in the product. At this time, however, it may be well to remind ourselves that we have here dealing with a situation where all of the ingredients are old. If an active ingredient is new, then this ingredient may be patentable as a new compound and the problem is automatically solved because a patent on a new compound covers all of the uses thereof.

So, let us consider the really hard problem where, as already stated, all of the ingredients are old.

Is there a possibility for protection of the process? It is not necessary, in order to obtain process protection, to employ a totally new process. In many cases, process protection can be obtained if it can be shown that the active ingredient, for example, was not employed in a particular type of composition before. As a hypothetical case, assume that compound X has been used as a froth flotation agent. We now find that it has a therapeutie effect when administered orally, without any solvents or diluents of any kind. It is theoretically possible these days to obtain a process patent reading something like the following:

> The process for combating athlete's foot which comprises administering X (our froth flotation agent) to a human being infected with athlete's foot.

Since there is no question about product or composition claims being more valuable in most cases than mere process claims, attention is next given to whether there is any possibility of obtaining the desired protection in our case where our composition consists only of old materials. Clearly, we cannot repatent an old product by itself. Consequently, our job is simply to set forth this old material plus at least one other material which is essential for the use in question. In the hypothetical case just given we are out of luck, as a practical matter, because X can be used by itself. However, in the great majority of cases analysis of the problem will show X

*Richards & Cifelli, Newark, New Jersey

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cannot be used by itself and therefore the problem is easy to solve. All that needs to be done is to recite one element which *must* be used in all cases.

A recent case which illustrates both the economic and the patent aspects of the problem involves Shell's well known TCP gasoline. The patent has not as yet been granted and all that is publicly known is the report of the case wherein the U.S. District Court for the District of Columbia reversed the U.S. Patent Office tribunals and held that gasoline containing TCP *and* a scavenger ingredient was patentable.

The Shell inventors had conceived the idea of using alkyl aryl phosphates, for example, tri cresyl phosphate, in gasoline, for the purpose of doing away with spark plug fouling. Actual tests demonstrated that this use substantially reduced the fouling of spark plugs, especially in connection with airplane engines. The product received widespread commercial acceptance throughout the world.

The Court in examining the prior art found that while it was very close from the point of view of showing phosphates including alkyl aryl phosphates in gasoline, nevertheless, it was not concerned with the problem of curing the fouling of spark plugs but was concerned with different problems such as the prevention of preignition and the problem of corrosion. Even so, the Court admitted that a certain Canadian patent, No. 421,568, disclosed a composition resembling the one disclosed in the Shell patent application. *However, the Court emphasized that a point of distinction was that the Shell inventors also had employed an additional ingredient operating as a scavenger and since no such element was disclosed in the Canadian patent the Court held that the combination disclosed in the Canadian patent is different from that disclosed in the Shell patent application.*

Applying the points made above, it will be seen that the Shell patent application by including the essential ingredient which operates as a scavenger (inasmuch as every internal combustion engine has an exhaust or scavenging stroke), a patentable distinction over the prior art was obtained.

The practical reasoning of the court is shown by the following quotation taken from the opinion:

> In dealing with this argument, it is well to refer to the opinion of Judge Learned Hand in Traitel Marble Co. v. U. T. Hungerford Brass & Copper Co., 18 F. 2d 66, 68. The same argument was advanced in that case. There the device of the prior art was very similar to that of the patent in suit, but the purposes for which the two inventions were used and the results that they obtained were entirely different and distinct. Judge Learned Hand made the significant remark:
>
> "*** but in view of the fact that McKnight's purpose and his result were quite different, structural distinctions which might be trivial became crucial.
>
> "Assuming, for argument, that the law is absolute that there can be no patent for the new use of an old thing, that is because the statute allows no monopolies merely for ideas or discoveries. If the thing itself be new, very slight structural changes may be enough to support a patent, when they presuppose a use not discoverable with inventive imagination. We are to judge such devices, not by the mere innovation in their form or material, but by the purpose which dictated them and discovered their function."

We cannot close our eyes to the fact that many great discoveries involve merely the development of a new and unforeseen use or result of an existing structure. While the law forbids the granting of a patent for such new use on the theory that patents are granted not for intellectual discoveries but for physical embodiments of such discoveries, nevertheless, as is indicated by Judge Learned Hand, when a new purpose is discovered, slight changes in the pre-existing device or composition of material may be sufficient to establish patentability, even if a similar difference without a change of use or purpose might not be sufficient.

The Court is of the opinion that the forward step taken by these inventors was far from obvious. The testimony establishes the fact that a very serious problem existed in the industry and that interested parties were looking for a solution; that the two inventors, who were experienced research engineers, undertook to try to find a means to solve the problem and that it took a couple of years of experimental work on the part of a group of trained men to arrive at a solution. The industry promptly accepted the result and has used it on a wide scale. Manifestly it cannot be said that the invention was obvious in the light of the prior art.

## RECENT PATENTS

***2,768,963*—G. D. Searle—Halophenyl - Hydroxy - Phenyl - Alkano-Nitriles.**

***2,768,970*—Schenley Industries—Phenyl - Styryl Ketone Thiosemicarbazones.**

***2,768,972*—Centre National de la Recherche Scientifique (France)—Preparation of N-Acyl-β Aryl-Serinols.**

***2,769,009*—Lepetit S. p. A. (Italy)—Isonicotinic Acid Hydrazones of Bicyclic Terpenic Ketones.**

***2,769,011*—C. H. Hacker—Chlorophyllin Derivative and Its Production.**

***2,769,014*—Polak & Schwarz's Essencefabrieken (Holland)—Process for the Prepn. of Novel Perfumes containing an M-Dioxane Ring.**

***2,769,019*—Upjohn—9 - Dehydrotestosterone and 9-Dehydronortestosterone and Esters Thereof.**

***2,769,020*—Schering—Process for the Isolation of 11, 20-Diketo Pregnanes and Products Obtained Thereby.**

***2,769,748*—Lever Bros.—Hair Dyeing Composition Comprising Polyhydroxyl Compound and Alkanolamine.**

***2,769,809*—Burroughs Wellcome—Triazines.**

***2,769,812*—Sterling Drug—1-Methyl - 2 - (3,3 - Diphenylpropyl) Piperidine.**

***2,769,817*—National Drug—Therapeutic Substituted Chalcones.**

***2,769,819*—Abbott Labs.—Alkylene-Diazides.**

***2,769,820-1*—Am. Cyanamid—1, 4-Naphthoquinoneimines.**

***2,769,837*—Sahyun Labs.—3,5-Diisopropylsalicylamide.**

***2,769,838*—Ciba Pharmaceutical—Polyglycol Ether Acid Amilides.**

***2,769,843*—Ruhrchemie AOH (Germany) Tricyclodecane-(5,2,1,0,$^{2,6}$)-Triol-(3,4, 8-9).**

***2,770,553-71*—Am. Cyanamid—Soft Gelating Encapsulation.**

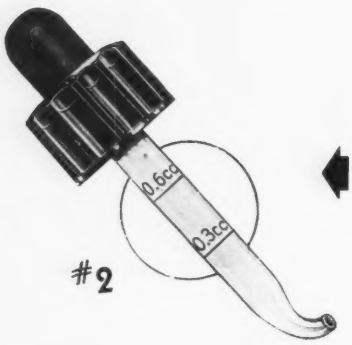
***2,770,568*—Boots Pure Drug—P-Chlorobenzyl P-Chlorophenyl Sulfide and Acaricidal Compositions Containing Same.**

***2,770,569*—Hoffmann - La Roche—Analgesics.**

***2,770,570*—Armour—Obtaining In-**

*(Continued on page 554)*

# *New Perfection* DROPPING PARTS

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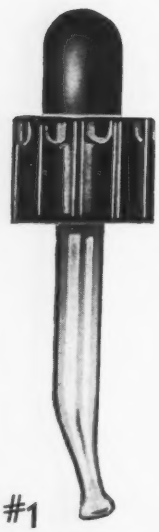

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Accurate calibration of New Perfection dropper glasses adds immeasurably to the user's satisfaction with your product. Not only is the specified dose measured with more precision, but the tedious and time-wasting practice of counting drops is made unnecessary.

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We can supply various colors of bulbs in natural rubber or in our special oil-resisting Amekine compound, caps of plastic or metal in many sizes and colors, and various types of dropper glasses in any length. New Perfection dropping parts will fit your own bottles, or can be supplied in combination with our Modernistic bottles in Amber, Blue, Green or Clear glass. Sizes: ⅛, ¼, ½, 1 and 2 oz.

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*"Glass Goods of the Better Kind"*

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# NEWS...

### Vitamin Foundation Officers

Dr. Russell M. Wilder, Professor Emeritus of Medicine, Mayo Clinic, has been reelected president of the National Vitamin Foundation. Dr. Robert S. Goodhart was reelected executive vice-president and scientific director.

Vice-presidents elected or reelected were: Dr. Warren M. Cox, Jr., technical director, Mead Johnson Laboratories; Dr. T. H. Jukes, Lederle Laboratories Division; W. R. McHargue, vice-presient, E. R. Squibb & Sons Division; J. J. Powers Jr., senior vice-president, Chas. Pfizer & Co.

Chairman of the board of governors is E. C. Kleiderer, executive director of development, Eli Lilly and Company; chairman of the executive committee, R. L. McNeil Jr., chairman of the board, McNeil Laboratories, Inc.; secretary-treasurer, J. David Hayden, R. P. Scherer Corp.; and assistant secretary, Rita D. Gilbert.

### Proprietary Assn. Meeting

The Proprietary Association will hold its 76th annual meeting May 12 to 15 at The Greenbrier, White Sulphur Springs, W. Va.

### Whitehall Exec. Vice-Pres.

Kenneth A. Bonham, assistant to the president of American Home Products Corporation, has been named executive vice-president and general manager of Whitehall Pharmacal Company, Elliott A. Bowles, president of Whitehall, has announced.

KENNETH A. BONHAM

### Lilly Board of Directors

J. C. Siegesmund, vice-president of engineering; G. B. Walden, vice-president in charge of biochemical manufacturing; and T. P. Carney, Ph.D., vice-president of research, development, and control, have been elected to the board of directors of Eli Lilly and Company.

Re-elected to the Board were: Eli Lilly, J. K. Lilly, E. N. Beesley, C. J. Lynn, N. H. Noyes, W. A. Hanley, F. M. Hadley, Forrest Teel, A. H. Fiske, W. M. Wheeler, Jr., C. R. Miller, and J. O. Waymire.

### Arctander Joins Colgate

Steffen Arctander, perfumer and chemist, has joined the Perfumery and Essential Oils Division of the Colgate-Palmolive Company. Regular contributor to scientific and technical journals and author of scientific articles on his botanical explorations

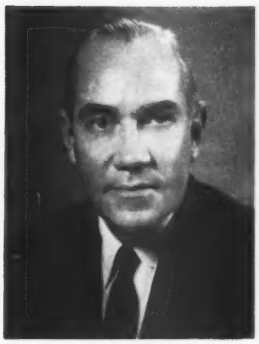
STEFFEN ARCTANDER

in Africa, he has made six trips to that continent to collect and photograph rare botanical specimens. He made his first trip to Africa at the age of 17.

Mr. Arctander was formerly chief chemist and perfumer for Co-Ro Manufacturing Company, Copenhagen, Sweden, his native country.

### Schering Sales Editor

Robert B. Beusse has been appointed to the newly created post of sales editor of Schering Corporation, according to an announcement by Herman W. Leitzow, vice-president. Mr. Beusse will use various media to develop a complete communications program linking sales management with the field organization. He will edit the "Detailer," a bi-monthly publication to the domestic sales staff and serve as advisor on professional and trade communications.



PAUL B. ROBINSON

### Warner-Chilcott Adv. Dir.

Paul B. Robinson has joined Warner-Chilcott Laboratories as director of advertising and promotion, it has been announced by Dr. Leonard A. Scheele, president.

### '57 Lederle Medical Faculty Awards Total $235,612

Grants totalling $235,612 have been made to thirteen outstanding medical school teachers and researchers by American Cyanamid Company through its 1957 Lederle Medical Faculty Awards. In making this announcement K. C. Towe, president, said that the awards, initiated by Cyanamid in 1954, were believed to be the first of their kind in the field.

"The basic purpose of the grants is to help assure to schools and universities adequate funds to encourage medical men of stature to continue in teaching and research posts," explained Mr. Towe. "The awards are intended to supplement existing salaries or to aid schools in filling positions with medical men of highest calibre."

The awards are administered and recipients chosen by an independent committee of professors from medical schools throughout the United States. All grants are for a term not longer than three years, and no single grant may exceed $10,000 per year.

### To Head Gordon Conferences

To head the Gordon Research Conferences this year are Dr. Robert W. Schiessler, who has been elected chairman of the board of trustees, and Raymond Stevens, who has been appointed chairman-elect. Dr. Schiessler is technical director of the Research Division, Socony Mobil Laboaratories, Paulsbora, N. J. Mr. Stevens is president of Arthur D. Little, Inc., Cambridge, Mass.

# Which qualities of **Baker** AMMONIUM CHLORIDE, U.S.P., Granular are important to you?

**HIGH PURITY—FREEDOM FROM EXTRANEOUS MATTER**

Baker Ammonium Chloride, U.S.P., Granular is a product of synthesis, manufactured in new and enlarged facilities. Purity is safeguarded in many ways—selected starting materials are reacted in specialized equipment in a completely closed system—filtered air is used in the production area—there is close process control at every point. Representative analyses show very low insoluble matter.

**DUAL-PURPOSE GRANULATION—FOR TABLETS OR LIQUID PRODUCTS**

The particle size is suitable both for direct compression into tablets and for rapid solution of liquid products. You eliminate duplicate inventories—and reduce production costs.

**EASY TO HANDLE FOR TROUBLE-FREE COMPOUNDING**

Special drying equipment, capable of close temperature control, assures low residual moisture (typically 0.1%). And thorough blending is another important step in achieving uniformity.

**PROTECTIVE PACKAGING**

Drums with polyethylene liners, filled directly from the blender, protect purity during transit and storage—help prevent moisture pick-up.

*Ammonium Chloride, U.S.P. is also available in Powder form.*

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**J. T. Baker Chemical Co.**

REAGENT • CHEMICALS • FINE • INDUSTRIAL

**Phillipsburg, New Jersey**

## Thomas Is Honorary Member Of Amer. Perfumers Society

H. Gregory Thomas president of Chanel, Inc., received an honorary membership in The American Society of Perfumers at its meeting held March 20 at Essex House, New York. The presentation occurred at the end of a symposium on the theme "What's Ahead in Fragrance?" presided over by Dr. Paul G. I. Lauffer, research director, House of Tangee. Mr. Thomas' talk "What's Ahead in Fragrance Types and Merchandising Methods?" concluded the program.

Other papers in the symposium were: "What's Ahead in the Perfumer's Art?," the Language and Indexing of Fragrance, by Camille H. Bourguet, American Aromatics, Inc.; "What's Ahead in Man-Made Odorants?," the Future of Creative Synthesis, by Harry C. Saunders, Givaudan-Delawanna, Inc.; "What's Ahead in the Science of Odorants?," Research Trends in Perfumery Materials, by Dr. Paul Z. Bedoukian, Consulting Chemist; "What's Ahead in Household Fragrances?," Odor Preferences Among Domestic Consumers, by Dr. Amos Turk, Consulting Chemist; "What's Ahead for Instrumental Analysis in the Perfume Industry?," by Dr. Ernst T. Theimer, van Ameringen-Haebler, Inc.

"There are no recognizable trends (in perfumes) in the same sense as we note trends in fashion," said Mr. Thomas, "True, there has been an increasing demand for stronger, heavier scents but only because the consuming public imagines these to be longer lasting and, therefore, better value for the money in the minds of those who are incapable of appreciating the refinements of a great perfume creation."

Attempts to describe perfumes are difficult, if not impossible, said Mr. Thomas. "All we have found we can say is that such and such perfume is flowery or oriental or mossy or light, or heavy or just modern (whatever this word may mean to the uninitiated). What all these terms reveal is the bankruptcy of our own descriptive powers. The language barrier stands against all our best advertising and publicity copywriting efforts."

Cited "for a lifetime in the course of which he has rendered so many eminent services to the cause of France in the United States and abroad in the field of economics and in the diffusion of French culture," H. Gregory Thomas, president of Chanel, Inc., was awarded membership in the French Legion of Honor at the March 14 luncheon meeting of the French Chamber of Commerce in the U. S. The newly appointed French Ambassador to Mexico, Count Jean Vyau de Lagarde, who made the presentation, smiles his approval as he admires Mr. Thomas' medal and ribbon. Looking on are General Marcel Penette, French Military Attache in the U. S., left, and Frederic Peter, Commercial Counsellor of the French Embassy.

Sales of perfumes have not expanded as quickly as other items in the field, such as lipstick and hair preparations due to the difficulty of advertising the non-visual effects of perfumes, said Mr. Thomas.

"It is harsh to say and hard to understand why so very poor a job has been done by the merchants of this country in promoting the use of perfumes," said Mr. Thomas. "Perhaps it is because the average cosmetic demonstrator in a department store or the average clerk in a drug store does not really understand very much about the perfume products which are offered for sale. More probably, it is because such understanding as does exist cannot find the proper words for sales expression."

"There are no real trends of perfume distribution to the super-markets," said Mr. Thomas, who concluded:

"In spite of the artificial obstacles placed in the way of its expansion by some nearsighted retailers, the perfume trade will still, and for a number of years in the future, be largely concentrated in the existing retail channels: The department stores, the specialty stores, and the drug stores of this country."

DR. GEORGE MAST

DR. PAUL WERMER

## In Key Warner-Chilcott Posts

Dr. George Mast, formerly vice-president and medical and scientific director of the Nepera Chemical Company, which recently merged with Warner-Lambert Pharmaceutical Company, has been appointed vice-president of Warner-Chilcott Laboratories and director of new product development.

Dr. Paul Wermer, who has been vice-president in charge of new product development, has been appointed medical director.

*the lipstick case*
*by PLUME & ATWOOD*

the **case** for quality; container division, the PLUME & ATWOOD MFG. CO., Thomaston, Conn.

## McKeen Heads Drug Division Of Medical Education Fund

John E. McKeen, president and chairman of the board of Chas. Pfizer & Co., Inc., has accepted the chairmanship of the Drug and Pharmaceutical Division of the National Fund for Medical Education, Colby M. Chester, chairman of the fund's Committee of American Industry, has announced.

The Committee is spearheading a nation-wide appeal to raise $10,000,000 each year for the country's 82 accredited medical schools.

In accepting the appointment, Mr. McKeen stated that his committee would seek to enlist the support of all pharmaceutical companies. He pointed out that industry has a responsibility to help medical education remain self-sufficient and self-reliant and called attention to the fact that the scientific advances emanating from medical schools have added twenty-one years to the average life span in the past 50 years.

Squibb "Knight of the Blue Vase" John Morian, right, looks on as his wife sips from the vase, traditional ceremony at the company's annual Gold Star Go-Getter banquet, held recently in New York City. Smiling approval are J. C. Leppart, far left, executive vice president, Olin Mathieson Chemical Corporation, and J. R. Watkins, Squibb field sales manager.

## Appointed by Squibb

James H. Douglas, former manager of E. R. Squibb & Sons' Indianapolis Division, has been appointed to the new post of promotion manager, merchandising products, in Squibb's New York office. Replacing Mr. Douglas in the Indianapolis division is Ivel H. Larmer, who has been serving as a clinical research associate for the company.

## Lilly Creates Agric. Res. Div.

Eli Lilly and Company has created an Agricultural Research Division. Previously, agricultural research was part of the Biochemical Research Division.

In announcing the change, T. P. Carney, Ph.D., vice-president of Lilly research, development, and control, named J. F. Downing, Ph.D., former head of the agricultural research department, as the new division director.

## Representing Florasynth

The Henry M. Rubin Company, Elkins Park, Philadelphia 17, has been appointed technical and sales representative for the masking agents and bouquets of Florasynth Laboratories, Inc, in eastern Pennsylvania, southern New Jersey, Delaware and Maryland.

## Union Carbide Appointments

T. F. Hart has been appointed product manger of silicone resins and sizings in the Silicones Division of Union Carbide and Carbon Corporation. M. H. Jellinek has been named product manager of silicone specialities, and R. S. Wishart Jr., product manager silicone fluids.

## Dr. Ruddy in New Post

Dr. Wayne Ruddy has been appointed director of organic chemistry of Warner-Chilcott Laboratories. Dr. Ruddy, who has been director of clinical development, will in his new position assume responsibility for both posts.

## Croda Officers Elected

J. M. Cannon, formerly vice-president of Croda Inc., has been elected president and treasurer of the company, according to an announcement by F. A. S. Wood, chairman of the board.

K. F. Neulinger has been elected vice-president in charge of sales, and Miss Y. Perlmutter has been elected secretary.

Lawrence H. Zahn, right, manager of methods and package development at Ciba Pharmaceutical Products Inc., is greeted by Administrator H. B. McCoy, of the Business and Defense Services Administration, U. S. Department of Commerce, prior to being sworn in as deputy director of the agency's containers and packaging division. Mr. Zahn is on loan to the Business and Defense Service Administration for a period of six months and will serve without compensation from the Government. Mrs. Zahn is standing at her husband's right.

# Givaudan gives you experienced help in perfuming men's toiletries

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The market for men's toiletries is a live, growing market . . . rich with opportunities for smart promotion. And the key to this market is fragrance . . . fresh, original scents that rouse masculine interest and respect, and stimulate men's natural pride in better grooming.

Givaudan has developed many fragrances that meet the challenge of this market . . . and we are prepared to help you develop special new scents that heighten and broaden the appeal of your products. We are also prepared to give you experienced counsel in solving any perfuming problems that may arise in the use of aerosol mediums, polyethylene containers and other packaging materials.

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*Better Perfume Materials Through Constant Research and Creative Ability*

**GIVAUDAN-DELAWANNA, INC.**
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## F. C. Brown Gets Hon. LL.D.

Francis Cabell Brown, president of Schering Corporation, was awarded the honorary Doctor of Laws degree March 25 at the Founders Day Convocation of Georgetown University.

Mr. Brown, a native of Washington, received the LL.B. in 1923, and the LL.M. in 1924, both from Georgetown. He has been admitted to practice in the District of Columbia, California and Nevada, as well as before the U.S. Supreme Court.

He conducted a general civil practice in San Francisco from 1924 to 1933, when he was appointed as counsel for the Federal Deposit Insurance Corporation. In 1941 he became solicitor for F.D.I.C., and in 1943 was named general counsel for that organization.

During 1941 and 1942, Mr. Brown served on a number of special assignments, making studies of property in the hands of Japanese-Americans evacuated from the Pacific Coast: formulating a program for replacement of drug supplies cut off in Latin-America by the economic blockade of Germany, and operating corporations seized under the Alien Property Law.

In 1943 he was appointed president of the Schering Corporation under the Alien Property Administration. Upon the sale of the corporation to the public in 1952, he was named chief executive officer.

Mr. Brown is a trustee of the National Foundation for Infantile Paralysis, and the Harry S. Truman Library. He is president-elect of the American Pharmaceutical Manufacturers Association.

## Berry Back from Fla.

Philip Berry, purchasing agent of Ungerer & Company, has returned after three weeks in Florida where he visited citrus oil firms.

ROBERT H. PULVER

JACK H. MOHR

## Ciba Sales Training Assoc.

Austin G. Peterson Jr. has been appointed sales training associate of Ciba Pharmaceutical Products Inc., it has been announced by Vincent A. Burgher, sales vice-president.

## Paul Kohnstamm Is Pres.

Paul L. Kohnstamm has been elected president of H. Kohnstamm & Co., Inc., succeeding Louis J. Woolf, who has been named chairman of the board.

PAUL L. KOHNSTAMM

Mr. Kohnstamm was formerly secretary of the firm and is a member of the board of directors. Elected to the newly created position of executive vice-president was Robert H. Pulver, member of the board of directors and formerly sales manager of the company's Mid-Western Division.

Arthur D. Vogel, formerly Eastern sales manager, was elected vice-president and member of the board. Walter J. Kohnstamm of the Chicago office, a member of the board and assistant treasurer of the firm, has been elected treasurer.

Robert A. Phair and Richard S. Carmel were re-elected vice-presidents. Elected to the board of directors were Richard L. Kohnstamm of Portland, Ore. and Herbert Haldenstein, New York City attorney.

## Mohr Heads P&T Division

Jack H. Mohr, former president of Lentheric, Inc., has been appointed to head the Toiletries and Dyestuffs Division of Park & Tilford. Fred Q. Swackhamer, for the past two years advertising director of Lentheric, has been named advertising and promotion manager of the division, and Wiley F. Patton, who served as assistant marketing director for Lentheric, has been appointed associate sales manager of the division.

## Hopkins Promoted by Becco

John R. Hopkins has been promoted to technical assistant to the sales manager of Becco Chemical Division, Food Machinery and Chemical Corporation, according to an announcement by Dewey H. Nelson, sales manger of Becco. This new position is designed to coordinate further Becco's technical service and sales facilities. Mr. Hopkins, formerly assistant manager of the southern territory, will move to Bacco's headquarters in Buffalo this Summer.

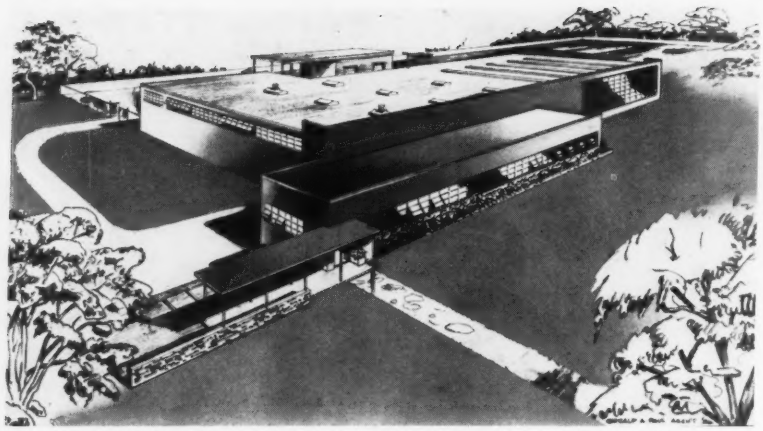
## Merck Asst. Secretary

Charles E. Childs Jr has been appointed assistant secretary of Merck & Co., Inc. by the board of directors. With Merck since 1946, Mr. Childs held several administrative positions before becoming assisant to the secretary of the company last May. During World War 11 he served as an officer aboard a U. S. destroyer.

## Schering Promotes Ingolia

Joseph J. Ingolia, former New Orleans division manager of Schering Corporation, has been promoted to field service manager, according to an announcement by Allan A. Miller, domestic sales manager of the firm.

ARTHUR D. VOGEL



American Cholesterol Products, Inc. has announced completion of its new plant and laboratory on twenty-acre Amerchol Park in Edison, N. J. Shown above is an architect's rendering of the 35,000 sq. ft. building, located on the main line of the Pennsylvania Railroad.

## Carroll, Serenbetz Join Vick

Albert Carroll has joined the Vick Chemical Company as vice-president of its Merrell-National Overseas Laboratories Division, it has been announced by E. P. Anderson, president of the division. Ray R. Serenbetz has joined the company as assistant to the president of its International Division, according to G. B. McClure Jr., division president.

Mr. Carroll was formerly vice-president and director of the Professional Marketing Division of Benton & Bowles and advertising director of Merck & Co., Inc. Mr. Serenbetz was formerly assistant controller of the International Division of General Foods Corporation.

## Chicago Perfumery, Soap And Extract Assn. Officers

E. F. LaSarre, managing partner of the St. Clair Specialty Manufacturing Company, has been elected president of the Chicago Perfumery, Soap and Extract Association. He served as vice-president in 1956 and as treasurer for several years prior to that.

Other officers installed are R. B. Harcombe, vice-president; W. A. Martin, secretary; and J. Baldwin, treasurer. Serving on the board of directors are the four officers and J. Helfrich, S. Olds, L. Haznaw, S. Lind, L. Keeper, K. Hartley, E. Esdale, H. Jelly, A. Culver, W. Frederickson and E. Kuehne

## Grove Dir. of Tech. Inf.

Efren W. Gonzalez has been appointed director of technical information services at Grove Laboratories, Inc., according to Dr. D. M. Green, director of research.

## CORRECTION

Drug & Cosmetic Industry
101 West 31st Street
New York 1, N. Y.

Gentlemen:

On page 407 of the March issue of "Drug & Cosmetic Industry" appears an advertisement from the Hotel Napoleon in Paris mentioning the name of Charabot.

There is no connection whatsoever, in any shape or form, financial or otherwise, between the Charabot Company and the Hotel Napoleon, or the Klaguine family, or Mr. Ivan Makowsky.

Yours very truly
CHARABOT & Co. Inc.
M. G. Couderchet
President

## Du Pont Div. Name Change: "Freon" Replaces "Kinetic"

"Freon" Products Division is the new name of the E. I. du Pont de Nemours & Company Organic Chemicals Department division concerned with manufacture and sale of fluorinated hydrocarbon refrigerants, aerosol propellents, solvents, and fire estinguishing agents. The change drops the Du Pont designation of "Kinetic" Chemicals Division, under which the "Freon" compounds have been made and sold since mid-1950, when Du Pont acquired all the assets of "Kinetic" Chemicals, Inc.

Du Pont officials have pointed out that while the name "Kinetic" was well known to older members of the refrigeration industry it holds little meaning for newer people in that business as well as in the ten-year-old aerosol industry, because it had never been used as a trademark on products. The trademark "Freon" has been applied to all Du Pont's fluorinated hydrocarbon compounds since their introduction more than a quarter of a century ago, and has come to be identified intimately in customers' minds with these products.

## Aromatics Division Formed By Hoffmann-La Roche, Inc.

Formation of an Aromatics Division has been announced by Hoffmann-La Roche, Inc. Sales manager of the new division will be Philip C. Burnham, formerly associated with R. W. Greeff & Company, who will take up his new duties next month. Burton T. Bush Jr., formerly associated with S. B. Penick & Company, has been appointed assistant sales manager.

K-V Pharmacal Company, formerly called Keith-Victor Pharmacal Company, and its New Products Division, Victor M. Hermelin and Company, have consolidated all their offices, plant and laboratory facilities in this specially designed new building at 2503 South Hanley Road, St. Louis.

## AFPE Officers

Howard B. Fonda, senior vice-president, Burroughs Wellcome & Co. (U.S.A.) Inc., has been elected president of the American Foundation for Pharmaceutical Education. Francis C. Brown, president of Schering Corporation, was re-elected vice-president of the foundation.

John J. Toohy, general manager, E. R. Squibb & Sons Division, was elected treasurer. James F. Hoge, Rogers, Hoge & Hills, was re-elected counsel, and W. Paul Briggs was re-elected secretary and executive director. L. D. Barney, president Hoffmann-La Roche Inc., was elected chairman of the finance committee.

The board of directors solemnized the passing of its sixth president, James J. Kerrigan, who died in office, September 5, 1956, and inscribed a Memorial Resolution to him in its permanent records.

## On Vitamin Foundation Board

Vice-president in charge of the Vitamin Division of Hoffmann-LaRoche Inc., Paul J. Cardinal has been elected to the board of governors of the National Vitamin Foundation. He has headed the company's bulk vitamin sales operations since the Vitamin Division was founded in 1939.

## Maltbie Opens Dallas Depot

Maltbie Laboratories has opened a warehouse and district office at 5610 Dyer Street, Dallas. L. V. Z. Brown has been named to manage the regional depot, which will service Louisiana, Oklahoma, Mississippi, Arkansas and Texas.

THOMAS R. DRINKWATER

## Appointed by U. S. I.

Thomas R. Drinkwater has been made assistant to the manager of alcohol and chemical sales for U. S. Industrial Chemicals Co., it has been announced by Alden R. Ludlow, U.S.I. director of sales. Mr. Drinkwater will assist Warren E. Johnson in managing the sale of U.S.I. industrial alcohol, solvents, and intermediates.

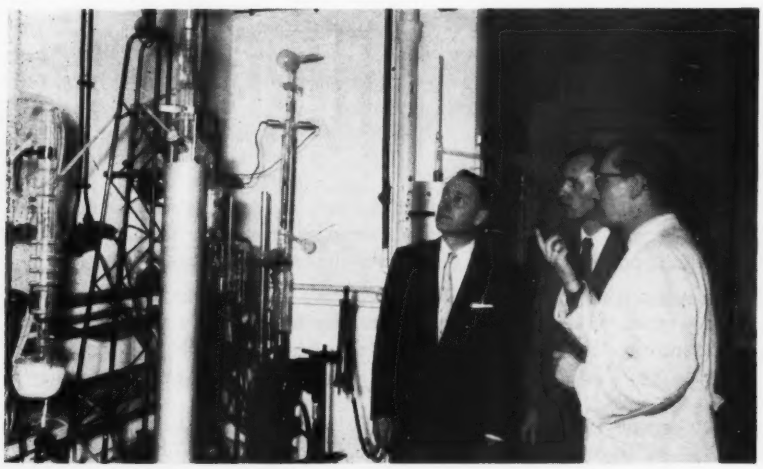
## C and C Promotes Dunn

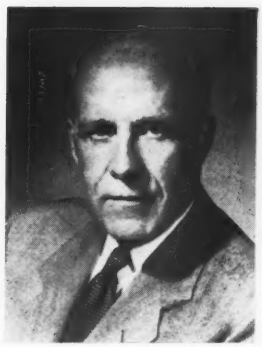
Dr. J. T. Dunn has been appointed assistant to Dr. Franklin Johnston, director of research for Carbide and Carbon Chemicals Company. Dr. Dunn started with Carbide in August, 1937, as a research chemist. He has worked in varied fields of chemical research with emphasis on acetylene chemistry. In 1954, he was promoted to group leader and held this position until his present promotion.

## Pierre Rougny Has Retired

Pierre Rougny, technical director and chief perfumer of Houbigant, Inc. for nearly 30 years, has retired.

Edward A. Bush, left, sales manager of Dragoco Inc., New York City, on a recent visit to the parent company in Holzminden, is guided on a tour of the plant by one of the Dragoco chemists and the firm's export manager for the United States.





JAMES V. O'LEARY

## CSC General Sales Manager

James V. O'Leary has been named general sales manager for Commercial Solvents Corporation, it has been announced by W. Ward Jackson, vice-president. Mr. O'Leary was formerly sales manager of the company's Biochemicals Division.

## Dingfelder in Europe

Sales manager of Felton Chemical Company, Inc., Adolph Dingfelder, accompanied by Mrs. Dingfelder, left March 16 on a six-week trip to Europe. He will spend one week at the company's manufacturing branch in Versailles, France and visit Felton sales representatives in England, Belgium, Germany, Switzerland, and Italy. Highlight of his trip will be his visits to the internationally important Hannover and Milan Fairs.

## Raymond Changes Name

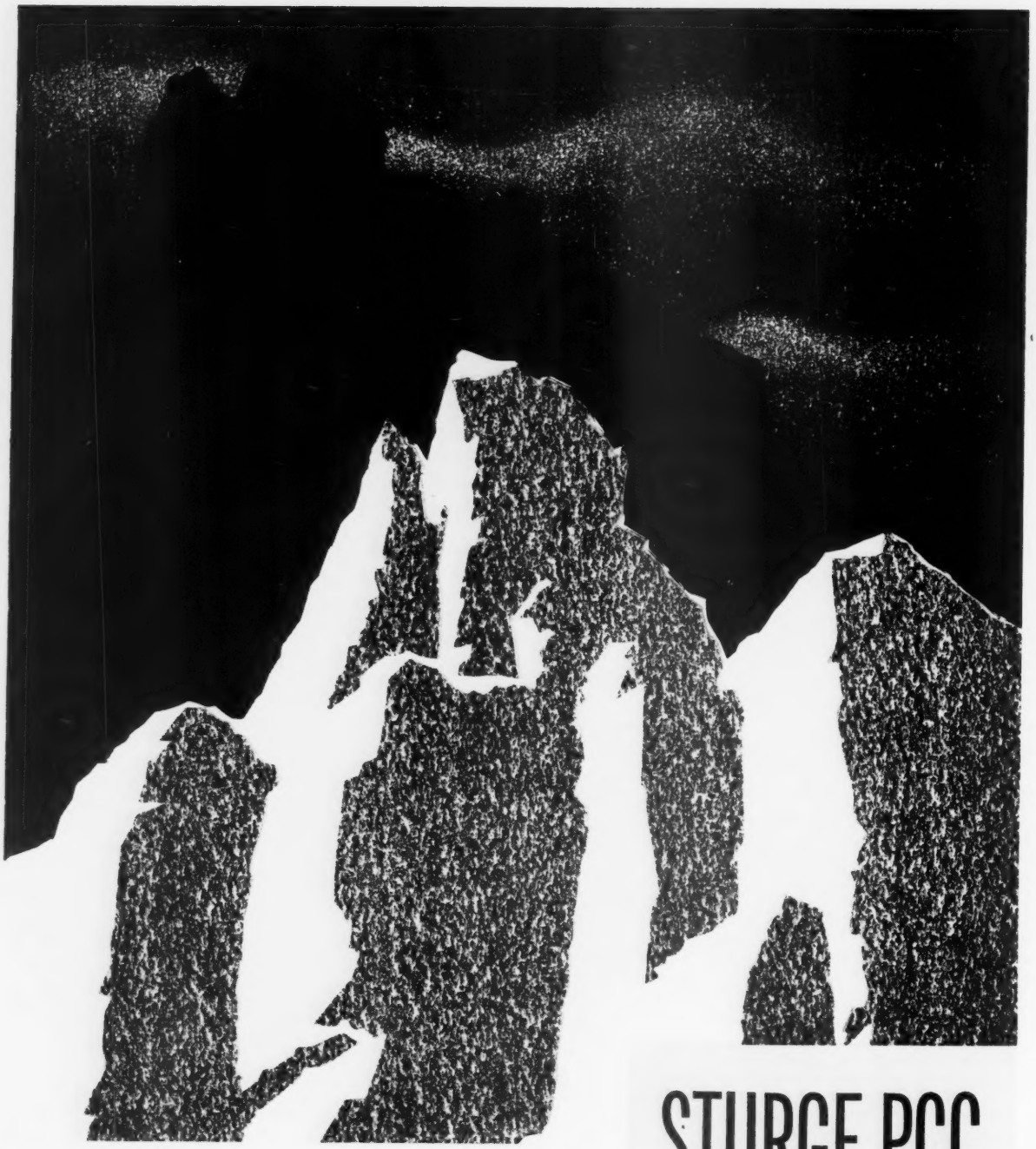
Raymond Laboratories, Inc., a wholly owned subsidiary of Rayette, Incorporated, will henceforth be known as Rayette, Inc., Chemical Division, by recent action of the parent company's board of directors.

Originally incorporated in August of 1951, the change in name was deemed desirable to associate more fully Raymond chemicals with the major trademark of the parent company.

Rayette, Inc., Chemical Division, will continue to manufacture and sell cosmetic grade raw materials to industry. Executive offices and manufacturing plants will remain in St. Paul, Minnesota.

## Bjorksten Appointments

James E. Henning has been appointed vice-president of Bjorksten Research Laboratories for Industry, Madison, Wisc. Irvin Leichtle has been named administrative assistant.



# STURGE PCC

**From a magic mountain a standard of excellence...**

From such pure limestone formations as this "magic mountain", John & E. Sturge Ltd., of Birmingham, England, manufactures precipated calcium carbonate. Sturge PCC has long been recognized as the world's standard of quality. Since 1823, Sturge PCC has been used in dentifrices, pill and tablet coatings, powders and fillers – wherever the best PCC is essential.

When you need a precipitated calcium carbonate that meets the most exacting specifications for texture, color and consistency – batch after batch – specify Sturge. Sturge's laboratories are available for studying any customer's problems. For a sample and information, contact H. J. Baker & Bro.

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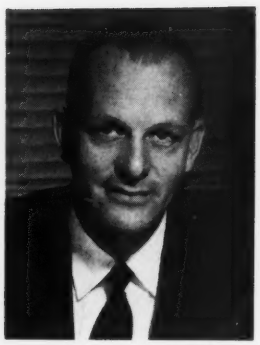

GLENN W. JOHNSTON

PIERRE T. DELEAMONT

HENRY F. MASO

### Williams Product Mgr.

Glenn W. Johnston has been appointed product manager for Williams Shaving Products, according to John E. Grimm, marketing vice-president of the J. B. Williams Company.

### P&T Appoints Miller

Carlyle E. Miller has been appointed general sales manager of the Toiletries and Dyestuffs Division of Park & Tilford, according to an announcement by Jack H. Mohr, general manager. Mr. Miller was formerly national field sales manager of Lentheric, Inc.

### On Mead Johnson Board

Dr. Ben King Harned, vice-president of research, and W. Paul Torrington, vice-president of manufacturing, have been elected directors of Mead Johnson & Company. Dr. Harned joined the company in 1952 as executive director of research, and was named vice-president in 1954. Mr. Torrington joined the company in 1942 as assistant to the president in charge of engineering. In 1948 he was named production manager, and in 1949, vice-president.

### Distillation Products Pres.

Graham C. Mees has been appointed president of Distillation Products Industries. He was formerly vice-president of sales for the vitamin concentrate producing division.

### Appointed by Mead Johnson

Donald E. Leslie has been appointed senior sales analyst in the market research department of Mead Johnson & Company.

### Secretary of Merrell

Raymond D. McMurray has been named secretary of The Wm. S. Merrell Company, Nelson M. Gampfer, president, has announced

### Firmenich Sales Rep

Pierre T. Deleamont has joined Firmenich & Co., as sales representative. A graduate of the University of Geneva, in Switzerland, he has been active in the perfume industry in Switzerland and the U. S. for the past eleven years.

### Newport Sales Manager

James J. Slattery has been appointed sales manager of Newport Industries Company, a division of Heyden Newport Chemical Corporation, R. J. Spitz, vice-president in charge of Newport domestic sales, has announced.

Mr. Slattery joined Newport in 1939 as a member of the sales department. Since 1942 he has been manager of Newport's Cincinnati district office.

Newport Industries Company has moved to Heyden Newport's offices at 342 Madison Avenue, New York.

### In Pfizer Research Posts

Appointed to managerial posts in the biochemical research and development department of Chas. Pfizer & Co., Inc. are Edwin J. Ratajak, who has been named manager of process improvement and development work; Dr. Gilbert M. Shull, who will direct work on fermentation chemistry, mycology and chromatography, and Dr. Ben A. Sobin, who will head the company's basic biochemical research.

### Proprietary Assn. Sec.-Treas.

James H. Merritt, executive secretary of the Ohio State Pharmaceutical Association, has been appointed secretary-treasurer of the Proprietary Association to fill the vacancy created by the death of A. K. Barta.

### B-M Brand Adv. Mgr.

John H. Tyner has been appointed brand advertising manager in the Bristol-Myers Products Division.

### Joins American Cholesterol

Henry F. Maso has been appointed director of technical services of American Cholesterol Products, Inc., it has been announced by Lester I. Conrad, vice-president and technical director of the company.

Mr. Maso, formerly senior research chemist at Johnson and Johnson, will direct American Cholesterol's customer service and product formulation for drug and cosmetic firms. American Cholesterol manufactures Amerchols, the emulsifiers derived from lanolin, as well as a group of emollient acetylated lanolin derivatives.

### Lilly Promotes Murphy

Hubert W. Murphy, Ph.D., has been named a pharmaceutical research associate by Eli Lilly and Company. Dr. Murphy participated in research which led to the determination of the structure of the erythromycin molecule. He has prepared and evaluated a number of new penicillin salts and worked on cellulose derivatives.

### Simon Lubarsky

Simon Lubarsky, 72, former president of International Vitamin Corporation, died March 14 in New York City.

A pioneer in the vitamin and drug business in New York, he retired in 1943 after thirteen years with International Vitamin.

### Robert L. Lund

Robert L. Lund, 81, former executive vice-president and director of Lambert Company, New York, and director of Lambert Pharmacal Company, St. Louis, Mo., died March 9 in St. Louis. He was president of the National Association of Manufacturers in 1932 and 1933, and board chairman in 1934 and 1935.

# Emulsifiers

For ease of use — For dependable results — For solving difficult problems

**Tegacid . . . . .** Glyceryl Monostearate—Acid Emulsifying. For anti-perspirant—deodorant creams, lotions and ointments—all greaseless, medicated formulations.

**Tegin . . . . . .** Glyceryl Monostearate—Self Emulsifying. For neutral greaseless creams, lotions, ointments, suntan creams.

**Tegin 515 . . .** Glyceryl Monostearate—Non Self-Emulsifying. Used in conjunction with auxiliary emulsifiers.

**Tegin P . . . . .** Propylene Glycol Monostearate—Self Emulsifying. For greaseless creams—brushless shave, foundation, suntan: lotions—foundation, suntan, ointments.

## Lanolin Absorption Bases

### Protegin X . . . . . Iso-lan

For Creams, Lotions, and Ointments

TEGOSEPT PRESERVATIVES
ESTERS OF PARAHYDROXYBENZOIC ACID

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CHEMICAL CORPORATION

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# Management Forum

*by Francis Chilson*
INDUSTRIAL CONSULTANT

### Difficult Design Problems

One of the most difficult problems encountered in designing a factory is that of bringing services to individual units of equipment. These services include one or more of the following: power, lighting, dust collection, compressed air, vacuum, water, steam and process lines. Necessarily all these services require ducts or piping of varying diameters. If the factory has a basement under it, all these services can be brought up through the floor wherever required. But a basement is more expensive to build than any other part of the factory especially if it is required that the factory floor be required to sustain live loads of 250 or more pounds per square foot. Even a crawl space is enormously expensive to build.

The manufacturing and packaging section can be gridded and all services put into floor ducts or channels. This also is expensive because the channels have to be specially framed out, waterproofed and covered with some sort of removable covers. And a grid system limits future equipment changes and additions to the grids.

The customary fashion is to bring all services down from the ceiling. This means a forest of pipes and ducts hanging from the ceiling. If a hung ceiling is used the service mains can be hidden above the ceiling but the drops will still be in evidence. They can of course be painted the same colors as adjacent walls and this will make them less obtrusive. I've tried grouping service lines and running them down adjacent columns or tall pieces of equipment. This doesn't help much when dust ducts are required because such ducts are apt to be pretty big. I experimented with the idea of a double duct; one section of which was to be used for collecting dust; the other to contain all other service lines. This never got beyond the exploratory stage because not all machines require all services and short drops would have been necessary in any case from the duct to the equipment.

The problem could be solved in single storey buildings if local business codes did not prohibit the use of concrete boxes such as are widely used in Mexico for building floors. These boxes are made in two halves each about six inches deep and the size of the boxes is about two by three feet. They are made of special cement under high hydraulic pressure and will carry loads far in excess of 450 pounds per square foot. When used as flooring the box halves are arranged in rows about six inches apart. Reinforcing rods are placed between the boxes. Service lines are installed, this being done by chipping holes in the ends of the boxes. The upper halves of the boxes are put into place above the lower sections and cement is poured between the closed boxes. When it sets a two inch topping is spread over all to form the finished floor. Removable cement tiles are left at intervals so that if it becomes necessary to add additional service lines they can be threaded through the boxes. In Mexico I was informed that these boxes are less expensive to use than solid reinforced concrete laid in the usual manner. But the manufacturer's representative told me his firm had little hope of ever getting the boxes accepted in the US. Up to now the firm has been turned down every time they have tried to get code approval.

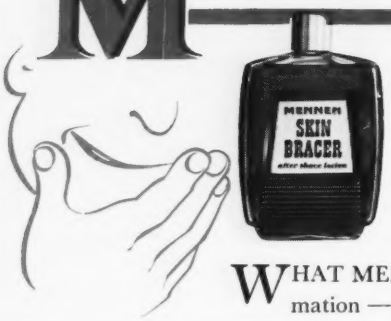
### Multi-color Factories

Long before the war I was sold on the importance of providing a colorful environment for factory and office workers, especially women. A colorful environment promotes alertness, efficiency and contentment. But I don't think we have yet gone far enough in using colors—bright colors. Many factory managers select a color combination and use it throughout the works. I think this is wrong. Every important area should be given a different color treatment, particularly the cafeteria and rest rooms, so that workers in passing from one area to another find themselves in a different color environment. I think we should go beyond even this and provide uniforms of different colors. There

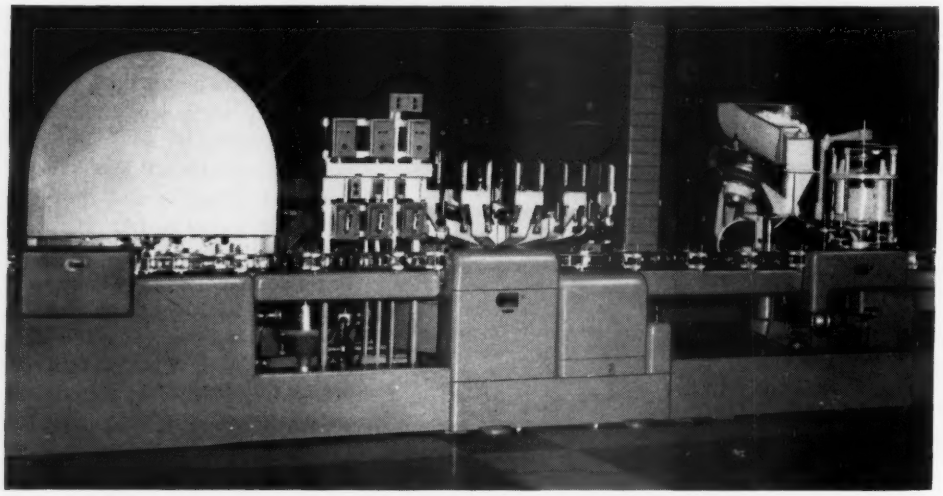
# MENNEN MAKES BOTTLING EASY-

## with PNEUMATIC machines

## "made for each other"




WHAT MENNEN's got is close to automation — a conveyor synchronized Pneumatic bottle cleaner, filler and capper! Capable of handling open-mouth as well as all glass sprinkler top bottles and the most delicately molded closures, it terminates in a fully automatic labeler capable of front and back simultaneous application.



A synchronous drive keeps the three machines, cleaner, filler and capper "in step" and in exact synchronism. The bottles pass from cleaner to filler and filler to capper without a hitch, and on spaced centers beyond the cleaner discharge.

Rounds, rectangles, or oval bottle sections are handled with ease. The capper is equipped with Sterling Cap Feeder especially designed for positive feeding without ever a possibility of breaking or marring.

The capping machine is equipped with sensitive chucks pre-set to any desired tension and this tension is maintained in day in and day out production.

The filler will fill light and heavy liquids equally well, alcoholic as well as oil base. It is designed for quick and thorough cleaning between fills on different products.

All of the equipment is designed to "go together" in a balanced, highly efficient, high productive rate unit. The brilliantly cleaned containers are exactly filled to the same height without dripping or messy spillage, screw caps are accurately and positively applied and the labels beautifully adhered to the containers without muss or misregistration. We'll gladly mail technical bulletins on any or all of this equipment — just write.

PNEUMATIC SCALE CORP., LTD., 70 Newport Ave., Quincy 71, Mass. *Also: New York; Chicago; Dallas; San Francisco; Los Angeles; Seattle; Leeds, England. Canadian Division: Delamere & Williams Company, Ltd., Toronto.*

★PNEUMATIC *Packaging and Bottling Equipment*

is no reason why girls in the same department shouldn't wear uniforms of a dozen different colors to suit individual coloring and taste, just as office girls do, who are not required to wear uniforms. Mixed colors should harmonize of course with the color of equipment, walls, columns and partitions. Hence the job of selecting the colors should be given someone who knows about color harmony. Factory uniforms, particularly for women, should be designed by a competent dress designer and not selected from the catalogue of a laundry supply company.

### On Getting Fired

Time was when Mr. Bigboss "looked down on you with his goddam wicked eye" as the old canal boat song put it, and you got fired for cause or no cause. But now-a-days Mr. Bigboss is a bit more careful. Executive personnel is hard to get and when you get it you may wish you hadn't. Many a man looks good in somebody else's stable but he develops spavin and glanders when he comes to eat out of your manger. So when Mr. B. gets sore at one of his lieutenants he doesn't fire the guy; he kicks the dog. Then he transfers the lieutenant to another job, sometimes one with a pompous title and no authority.

Getting "kicked upstairs" is a very familiar saying these days. Many executives are very skillful in avoiding situations that might bring them under Mr. B.'s baleful scrutiny. Sometimes Mr. B. himself won't drop the reins when his own time comes. He becomes chairman of the Board. Then when the succeeding president reaches retirement age, he becomes chairman of the Board and Mr. B. chairman of the executive committee or a consultant to the Board. When you've got your feet in the trough it's hard to take them out. When you're in a position of power it may not be easy to fire one of your colleagues but it's a damn sight harder to fire yourself.

### Plant Site Topos

Little can be done in laying out a new plant site without a topographic map. But the topos required for general site layout and the building itself are entirely different. For general layout purposes a 25 foot interval will do. But the area of the building will require a two foot interval. That will have to be done by a surveyor. All topographic maps are expensive if you have to hire surveyors to do them. It's a time consuming, meticulous job. I found a short cut which gives me what I want for a couple of dollars. You can get from the Geodetic Survey a topographic map of the township in which the site is located for a dime. The scale is too small to use, being one inch equals 66,000 feet. Outline the plant site on this map and have a photostat made at one inch equals 660 feet—the standard surveyors scale. The negative costs about $2.00 and the prints about a quarter each.

You can use the prints for layout work. But if you are fussy and don't like the fuzzy topo lines the blow up will give you, you can have a draughtsman make a a tracing from one of the prints. Also from the Geodetic Survey you can get an aerial photograph of the area for a dollar each. These aerial survey photographs are made with stereoscopic mapping cameras at a constant elevation and direction. They are exactly the same scale as the blown up photostats of the topo: one inch equals 660 feet. Thus for an expenditure of less than ten dollars you can have a topo which will show ever contour and all buildings, railroads, roads and other structures in the area. The photographs will show everything including the trees, and if you can read a reconnaissance photograph, you can identify the trees—so sharp are these photos. Of course I am talking about the Eastern area. The Geodetic Survey began making these photographic surveys right after the war and the intention was to cover the country. Just how far the job has progressed I cannot say. These photos are all numbered and each one covers an area of about four square miles. So if the line of the survey happens to have been through the center of your property, you may have to buy two or three and match them up. If you want a cheap aerial photograph of your present plant this is a way to get one.

### 1957 Styles

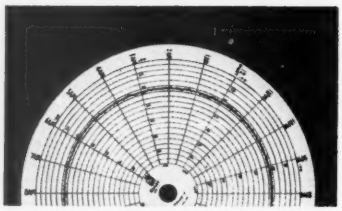
I am amazed that the Big Three automobile manufacturers allowed their designers to put the brakes on their business. When I saw the first '57 models I instinctively felt that the public wouldn't go for them. I wrote a letter to that effect to one of the financial papers predicting that the automobile business would be off at least 30 per cent in 1957. The new models are ridiculous:—one third trunk, one third hood and one third uncomfortable passenger compartment. The bright boys in Detroit didn't realize apparently that the automobile is in America no longer an item of social prestige. When they began making the so-called low priced cars look as big and as fancy as the high priced ones, they killed the goose that laid the golden egg. Nobody gives a damn now what kind of car his neighbor has or how many of them. He simply wants transportation. And that I think explains the increasing popularity of the small low priced foreign cars—that and the increasing price of gasoline. The automobile industry simply got too damn big for its britches. The industry is beginning to find out that sales can be forced up to a point. People will pay up to a certain amount for a flashy package but beyond that they balk, and they have balked as the reports and the loaded car lots show. I know several people in the trade who refused to take the new Cadillacs even though for years they have traded every year. I was going to buy a new car until I saw them and then I balked too. What America needs is a new Model T. I remember a cosmetic house at the end of the war which made a terrific furor with flashy advertising,

WEATHER WATCHER AT WORK

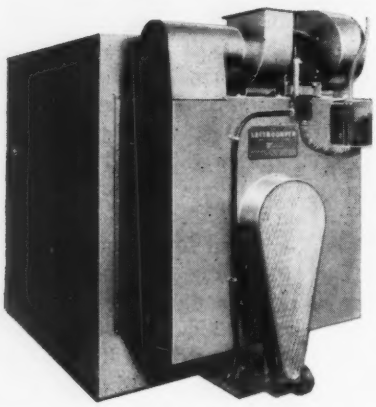
# How the weather watcher lost his job

HE KEPT AN EYE on the humidity—said when it would be safe to run and when to shut down. Operations were pretty sketchy during humid summer days, until they discovered that a Lectrodryer makes them independent of the weather. Now they work every day, regardless of the humidity.

## Their dewpoint recorder now shows constant DRYness



This is a true story—happened in a candy factory in Chicago. But it's one that's been repeated hundreds of times all over the world—in every type of plant where unwanted moisture is present in air, gases or organic liquids.



## Air-drying Lectrodryer

If you're tired of seeing high humidity gum up your production, send for the booklet *Because Moisture Isn't Pink.* It tells how other weather watchers solved their moisture problems. Write Pittsburgh Lectrodryer Division, McGraw-Edison Company, 309 32nd Street, Pittsburgh 30, Pennsylvania.

**Lectrodryer**

*REGISTERED TRADEMARK U. S. PAT. OFF.

flashy packages and flashy prices. When little but cosmetics and perfumes were obtainable as Christmas presents, this company did a whale of a business. But when simple stuff in simple packages at reasonable prices began to be available again, the bubble burst and the company blew up with it.

### The Old Order Changeth

Elihu Root and Theodore Roosevelt were fishing one day, so the story goes, and Root asked TR how long he thought democracy would last in America. Roosevelt is said to have replied, "Not over fifty years." The fifty years are up and we still have democracy of a sort but in the sense of personal liberty we are losing it fast. The State is closing in. I was reminded of this when I came home one day recently and found that one of the contractors of the Albany-Boston Throughway, which is one day to pass through my land, had entered my property cut down several stately specimen lawn trees that took a half century of slow growing to produce, and bulldozed out a hedge of lilac bushes, without so much as "by-your-leave."

I understand the law of eminent domain. I understand that progress cannot be stopped. But I do not understand a law—and it is a law—which permits the State to enter private property and begin tearing it up even before negotiations have been initiated to purchase or condemn the required land.

Why should the State arrogate to itself the right to determine that a new road is needed from Albany to Boston or from Hell to Hackney? In my particular case this is a million dollar a mile road—undoubtedly the most graft ridden project I have ever encountered. For example an overpass is to be built near my land at a cost of a quarter million dollars for the benefit of eight families, all of whom have other means of egress to the north. It smells. I fought it and got exactly nowhere. Because nobody gave a damn.

Where is that spirit of violence and blood letting which Thomas Jefferson thought necessary for the preservation of democracy? Gone. All gone.

We submitted like sheep to the income tax, to the draft in peacetime, to social security, and like sheep we will be led—who knows whither?

### Clerical Work

According to the Wall Street Journal many big firms are conducting campaigns against superfluous paper work along the lines suggested on many occasions in this department. We are living in an age of paper. We are smothered with it. I have no hope that we will ever get our heads above it. Time and again I have urged clients to cut down the number of their records, to eliminate and combine forms, to regulate red tape making procedures. But I've given up. One mess gets nicely cleaned up but a year later all the red tape is back plus a lot more. We rail against bureaucracy in government and do nothing about it in our own businesses. About eighty per cent of the crap that gets so carefully filed should never get into the files at all. But it does. And it will. For years I've tried to get executives to tell their secretaries when to make carbon copies of letters and when not. But they forget and the girls do the copies automatically. They're trained that way. And the copies are religiously filed. Take the silly business of writing a letter. The envelope contains the name, company and address of the correspondent. For no reason at all this is repeated at the beginning of the letter when all that's necessary is the man's name and company. Then you salute him as "dear." (In some cases you write "dear" when you'd prefer to say "You SOB!".) Salutations are silly. Likewise the terminal "yours very truly." I wonder how many billion times that is written every day? For what reason? None. Just the fringe on the red tape. But oh, mein Gott, the cost!

### Middle East Mess

There is no doubt but that we are and will continue to be living in an era of big nations. Splinter nations are passé. Economics and the atom are the primary amalgamating forces. The idea, promulgated by Woodrow Wilson, that, just because a few people with a common lingo happened to stick together (usually they were too poor or too damn lazy to go anywhere else), they are entitled to the right of self determination has brought much evil to the world. Where is the line to be drawn? Take Brooklyn for example. Brooklyn has its own language and a few peculiar customs. Why shouldn't Brooklyn become an independent nation? Or Minnesota? There are more Swedes in Minnesota than in Sweden. But the idea of self determination has spread like fire across the world and you now have the spectacle of artificial little nations telling Uncle Sam to go to hell. There was peace in the world when England was its policeman. When little pipsqueak nations got rambunctious England moved in and spanked a few bottoms and that was the end of it.

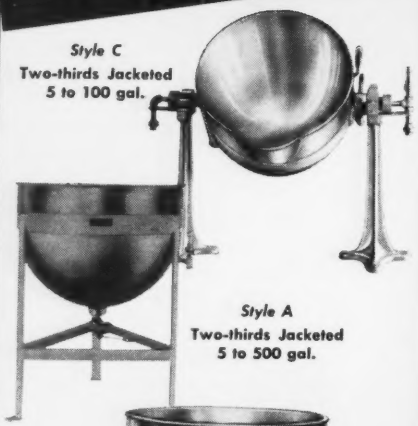
### Gadgets

The last word in gadgets is utilized in one of the local aromatic chemical plants. Every supervisor has a miniature short wave receiving and sending set attached to his belt. Each set has its own wave length. When a bloke is wanted the telephone operator signals him and they have a nice comfy chat. Obviously the bigboss loves gadgets.

### Skeletons Out of Closets

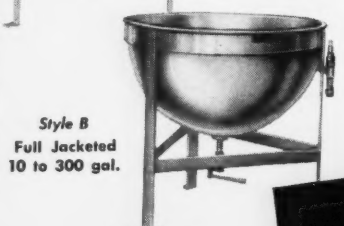
I have just discovered how Herbert Stearate Bye—'Erbie to his friends—the genial president of M. W. Parsons-Plymouth Inc. acquired such prominent calluses on his backside. Barnacles, they are, God's truth! 'Erbert maintains that a man never properly learns the art of selling until he has accumulated a collection of horny protuberances

## COOKING KETTLES

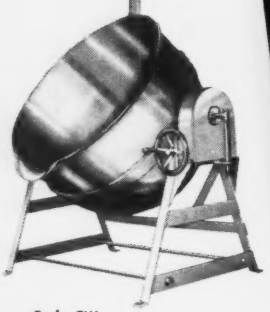


*Style C*
Two-thirds Jacketed
5 to 100 gal.

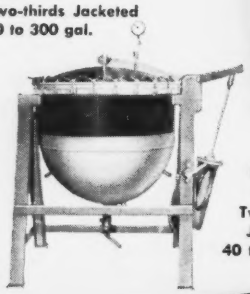
*Style A*
Two-thirds Jacketed
5 to 500 gal.



*Style B*
Full Jacketed
10 to 300 gal.



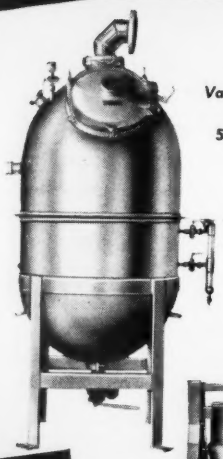
*Style CW*
Two-thirds Jacketed
80 to 300 gal.



*Pressure Kettle*
Two-thirds Jacketed
40 to 200 gal.

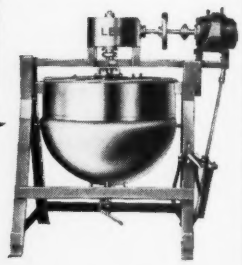
## MIXING AND BLENDING UNITS

*CW3T*
*Center-line Scraper Agitator Kettle*
80 to 300 gal.



*Vacuum Pan*
50 to
500 gal.

*D3T*
*Center-line Scraper Agitator Kettle*
25 to 300 gal.



*Quick Cooling Pan*
50 to 200 gal.

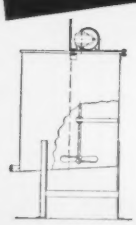
# *these* LEE Units

## WILL REDUCE YOUR PROCESSING COSTS!

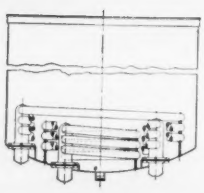
Individually designed for a specific processing operation and available in a wide range of sizes to fit your exacting requirements, Lee corrosion-resistant equipment is built to give you long years of peak performance with minimum maintenance.

Descriptive bulletins are available for any or all of the above units. Write for them today and discover how Lee can help reduce *your* processing costs.

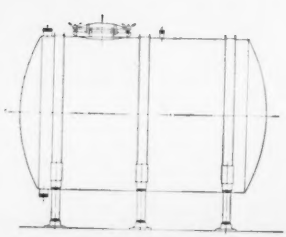
## MIXING, COOKING & STORAGE TANKS



*Mixing Tank*
25 to 500 gal.



*Pulp Tank*
500 to 2,000 gal.



*Storage Tank*
100 to 5,000 gal.

**LEE METAL PRODUCTS CO., INC.**

**408 PINE STREET,**
**PHILIPSBURG, PA.**

ALL LEE KETTLES ARE MADE TO A.S.M.E. CODE

on his butt. 'Erbie got his in the early twenties when he came over here from England with the intention of remaining permanently. He had been here for a time before World War I but went back to fight the Huns. With the war behind him he got a job selling some sort of lubricants to the gas stations and garages around the west side of New York. Then these establishments were owned mostly by Irishmen, and, as you may recall, the Irish freedam agitation was in full swing. Lord Mayor McSweeney was dying of a hunger strike in an English-controlled jail in Cork. The Sein Fein movement was at its height, in this country as well as in Ireland, and the Irish garagemen were all Sein Feiners.

Can you imagine 'Erbie with his monocle and impeccable Oxford accent calling on a bunch of bellicose Irishmen? The moment he'd open his mouth a couple of micks would grab him and toss him AOH out of the door and he'd skid across the pavement on his rear end and into the gutter. Do you suppose that disturbed his aplomb? Not on your life! He'd pick himself up, adjust his monocle, brush off his plus fours and yell at the Irishmen, "I've bee-en thrown out of better bloody places than yours!" Then he'd run like hell down the street. But did this sort of treatment affect his sales persistence? It did not. Like all true, bull-headed Englishmen he'd try again at the very next garage he came to. Whereupon the process would be repeated.

When you've been thrown out of many places and kicked out of an equal number, you're bound to grow calluses on your rear end. 'Erbie is proud of his calluses. 'Scars of battle' he calls them. He'd like to exhibit them publicly but he's a bit on the modest side. Anyway the accumulation of these barnacles made a great salesman out of him. One would suppose that he'd have thought of greasing his rear end with some of the lubricants he was trying to sell. But he didn't. He insisted on selling the stuff, not using it. 'E's a singleminded person –'e is. Cor! 'Erbert doesn't wear his monocle any more. He says he found he couldn't hear as well with one eyeglass; so now he wears two.

### Seek Fool-Proof Compression Coater

The University of Michigan College of Pharmacy is participating in research on a new, fool-proof compression tablet coating machine which may lead to a major change in the manufacture of pills.

According to Albert Mattocks, professor of pharmacy, until recently all tablets have been coated or covered by revolving them in deep pans, cement mixer style. This process is lengthy and requires skilled labor. While tablets are well coated, there is considerable waste material. Compression coating was introduced on a large scale about five years ago with machines that could stamp out 400 pills a minute.

The trouble with some present pill-making machinery says Mr. Mattocks, is that there is no way of checking to be absolutely sure the finished tablet has an active ingredient core inside.

"A tablet with no core has no therapeutic value," he observes. "Some manufacturers put iron in the core, then inspected the pills with a magnet. The problem with this was that some people cannot tolerate iron. The use of opaque material which permits tablets to be checked by x-ray has also encountered opposition."

The machine which the College of Pharmacy has helped develop will produce 1,000 coated tablets a minute, every one with an active ingredient core. Its secret is suction.

Active ingredient cores are picked up by vacuum suction tubes and transferred to the compression chamber. If a tube fails to pick up a core, the vacuum simply sucks up the granules out of the die that otherwise would have made up the coating and deposits them in a collection can. There is no possibility of a tablet being compressed without a core, says Mr. Mattocks.

Commenting on the interest of the college in this machine, built by the Arthur Colton Company of Detroit, Professor Mattocks adds, "We feel this type of tablet coating will become the basic process in the future. Now that the machine has been developed, a great deal of work is needed in the laboratory. The development of new types of products such as this, the making of granules for coating, and other steps will all require new technical knowledge.

"Our main interest is in developing this new knowledge and preparing people to utilize it in full. We are assisting the Colton company in working out some of the technical problems of this new machine, such as the exact size and type of granule needed for this very different type of coating process."

In addition to its speed and reliability, he notes, the machine makes it possible to use different coating on the top and bottom of a pill, permitting separation of materials which would otherwise react to each other. If desired, several coatings can be applied to make pills within pills. In this case, the original coated pill becomes the core for a larger pill. The complete reliability of the machine in making sure that each pill has its ingredient core eliminates the need for inspection.

Among the advantages of coating tablets which the professor cites are:

1. Pleasing appearance of the finished product,
2. Covering a bitter taste of ingredients,
3. Protecting active ingredients from oxidation or exposure to moisture, and
4. Fulfilling medical needs.

Vitamins, the professor notes, come in a wide variety of colors which would present an unpleasant appearance without coating. Coatings can be used to keep a pill from breaking up until it goes to the

intestines, or be used in layers to release different ingredients at various time intervals.

Penicillin was one of the first of the newer drugs to be compression coated. Normal pan coating could not be used because the heat involved in this process decomposed the drug. Professor Mattocks believes the speed and reliability of the new compression machine will very likely result in a cheaper process than pan coating.

Editor's Note: *The widespread interest of the trade in compression coating is interesting and belated in view of the fact that Francis Chilson successfully coated Grove's Bromo Quinine tablets in 1932. The procedure was described subsequently in two articles which appeared in this column before the war. But at that time there was no reader response.*

### Palletless Handling

Handling normally palletized goods without the aid of pallets is possible with a new multiple attachment developed by Lewis-Shepard Products, Inc., Watertown, Mass. For use with Lewis-Shepard Model "E" Trucks, the attachment consists of multiple forks, side-shifter and push-off device. It is especially effective where complete selectivity of each unit is desired, and when individual unit loads are moved directly from storage to the outbound highway trailer or freight car.

In a typical industrial operation, goods might be flowing off a production line. Instead of being palletized at the end of the line, they would be received and stacked on a multiple-prong device.

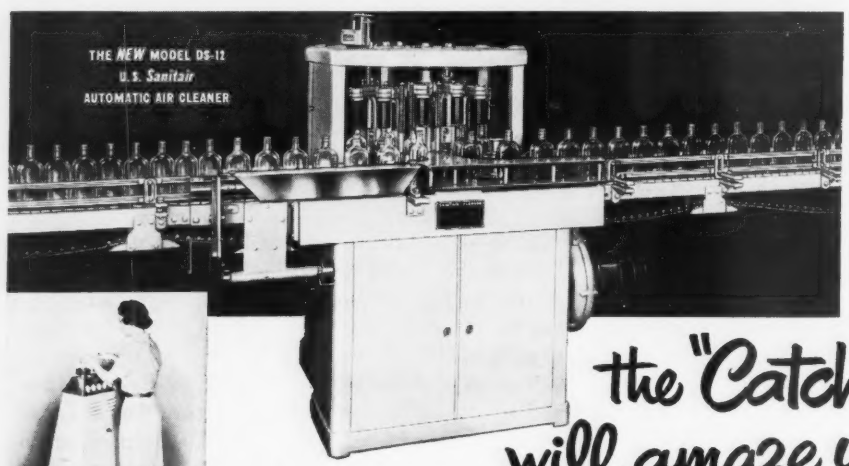
To pick up the load, the fork truck operator simply inserts his truck's six forks between the prongs and raises his forks. With the load now on his forks, he travels to the storage area.

At the storage section, he deposits his load on special all-steel storage racks, also produced by Lewis-Shepard Products, Inc., for use with this palletless handling system. The racks are of cantilever-type construction. To facilitate the placing and removing of loads, the multiple forks easily slip between the individual length-wise beams of the racks.

When a load is to be taken to an outgoing motor truck or railway boxcar, the fork truck operator proceeds to the appropriate storage rack. After simply slipping the forks between the cross beams of the racks and raising the load, he transports it to the outgoing carrier.

He deposits the load in the carrier just by pushing it off the forks with the push-off device, a plate normally located at the rear of the forks. He can either place the goods on the floor, or stack them atop other articles.

Lewis-Shepard also offers a side-shifter attachment on the trucks, which makes possible horizontal movement of the forks to further ease placing and removing goods from the racks. Controls for the attachment are located adjacent to the vehicle's main controls.

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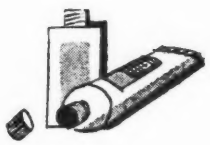


# Advancing Therapy

## Protein Nutrition Conference

The importance of high quality protein in the diet and its effect on disease was discussed at a two-day Conference on Protein Nutrition, cosponsored by The New York Academy of Sciences and E. I. duPont de Nemours & Co., Inc. Dr. Genevieve Stearns, University of Iowa, said that children from 18 months to four years should receive three to four grams of protein daily for each kilogram of body weight because skeletal musculature growth is most rapid at this age. As the child grows older a level of two and one-half to three grams should be maintained for muscle growth and to allow excess for recovery from common febrile and other illnesses.

Tuberculosis has less chance of reactivation in adolescence and rheumatic fever patients recover faster if they have been receiving adequate high quality protein, Dr. Joseph A. Johnston, Henry Ford Hospital, Detroit, reported. Protein should comprise 15 per cent of an adequate caloric intake. Because the onset of sexual maturity imposes a nutritional strain on teen-agers, he urged the National Research Council's recommended protein allowances be raised.

Severe protein deficiency, the most important single nutritional disease in the world today, can be treated by fortifying diets. Dr. James Hundley, United Nations Children's Fund, told the meeting that deodorized fish meal, soy milk, and peanut, sesame and cotton seed flours are possible high protein supplements for cereal foods. Dr. Federico Gomez, Mexico City, described successful treatment of severe protein malnutrition by fortification of a native corn meal and beans diet with the synthetic amino acids lysine and tryptophane. These results, obtained in a small group of children with kwashiorkor, have prompted further investigation, Dr. Gomez said.

The conference, which heard some twenty other nutritional scientists, was chaired by Dr. Fredrick J. Stare.

## New TB Antibiotic

Discovery of a new antibiotic which has shown itself to be highly effective in destroying tubercle bacilli was announced in a series of three papers presented at the 16th Veterans Administration—Armed Forces Conference on Chemotherapy of Tuberculosis.

The new drug, Dalacin, has undergone extensive tests in the laboratory in vitro and in mouse tuberculosis. Clinical trials to measure its efficacy in human tuberculosis are now under way.

Drs. Paul Siminoff, Robert M. Smith, Walter T. Sokolski and George M. Savage, reported that streptovaricin (generic name of Dalacin, which is an Upjohn trademark) is active against a wide variety of bacteria. Its activity against the tuberculosis organism is particularly striking.

They noted that under similar test conditions, Dalacin proved itself about 10 times as active as streptomycin and about 100 times as active as para-amino salicylic acid (PAS)—two drugs used widely in tuberculosis therapy.

They found that it was only half as active as another widely used agent, isoniazid. They added: "Streptovaricin is not cross-resistant with streptomycin or any of the commonly employed antibiotics."

Studies of the drug in the tuberculous mouse and guinea pig were reported in a second paper by Drs. L. E. Rhuland and Kurt F. Stern. They noted that streptovaricin was tested against two highly virulent strains of the tuberculosis organism—one human and one bovine—in experiments with mice., Against both strains, they found, the drug gave "100 per cent protection to mice . . . at daily doses of 200 milligrams of the drug per kilogram of body weight of the mouse."

Other animal studies with the drug were described by a research group from New York Hospital—Cornell Medical Center, New York. They reported that Dalacin showed a remarkable ability to potentiate the striking power of isoniazid in attacking the tubercle bacilli.

Dr. Robert McCune and Kurt Deuschle, reported for the group, which includes Drs. Walsh McDermott, Carl Muschenheim, Roger Des Prez and C. Jordahl.

Results of preliminary clinical studies with Dalacin alone on 17 cases of advanced pulmonary tuberculosis, however, were not dramatic, they added. The Cornell group is presently conducting a more extensive clinical trial to study the combined effect of isoniazid and Dalacin.

A fourth paper, describing the isolation and chemical properties of streptovaricin, was presented by an Upjohn team which included Drs. George B. Whitfield, Edward C. Olson, Ross R. Herr, John A. Fox, Malcolm E. Berg and Gerald A. Boyack.

## Race Track Medicine

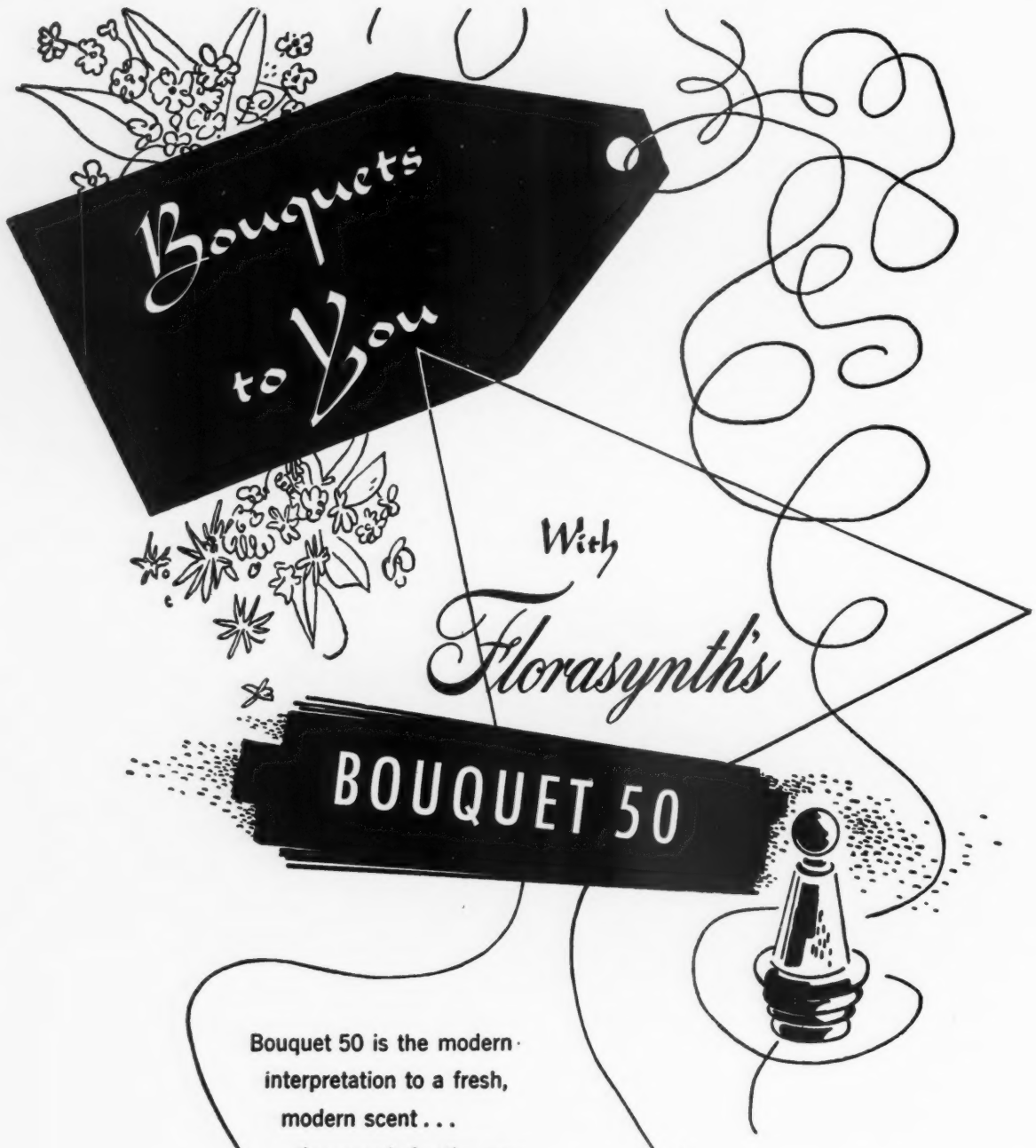
Among the many products mentioned briefly in this paper by N. E. Roberts (*Calif. Vet.* 9:19, 1956) are the following:

Vitamin B complex is used by the author as a tonic and appetite stimulant when horses are in hard training; no vitamin will increase the speed or stamina of any horse, regardless of how much or when it is given.

Cortisone and ACTH have been largely replaced by more effective drugs. ACTH is of some benefit in certain back lamenesses, and it is also used for animals that do not respond to vitamins as an appetite stimulant.

Intravenous hydrocortisone is very effective in the treatment of shock, acute inflammations, and allergies.

Prednisolone is an extremely versatile drug, and the author now uses it intra-articularly and intramuscularly in all cases where a steroid is indicated. Com-

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pared to hydrocortisone and cortisone, its effects last longer, it produces more pronounced relief, and a small dose is required.

Reserpine is principally used on unruly and vicious animals as a means of restraint, and it also is valuable in the treatment of stall-weavers or other highly nervous animals and of difficult shippers. Since it depresses muscle function, it has rather limited use on horses in heavy training.

## Proclorperazine

Proclorperazine (*Compazine, S.K.F.*), a recently developed analogue of chlorpromazine, shows great promise according to T. J. Vischer (*N.E.J. Med.* 256: 26, 1957) in the treatment of the mild mental and emotional disturbances commonly seen in everyday practice and treated on an ambulatory basis. It is particularly valuable for the many cases in which psychoneurotic symptoms make treatment of the primary disease less effective.

In this preliminary clinical study 21 of 38 mildly disturbed patients seen in general practice were afforded total symptomatic relief, and 16 were partially relieved. In one case proclorperazine produced little improvement, but this was a long-standing case of involutional melancholia, relieved temporarily only by electroshock therapy. The complete absence of side effects, except mild drowsiness, was most gratifying. In most cases patients treated with proclorperazine showed prompt and marked improvement in emotional outlook.

## Iron Deficiency

Anemia due to iron deficiency is a problem in the United States and other countries having high living standards, a group of hematologists and nutrition-minded physicians agreed at a symposium sponsored by the University of California extension division.

The disorder apparently is widespread among children six to 18 months old. It also is prevalent among pregnant and multiparous women and is likely to be an aggravating factor in any condition or trauma that results in blood loss.

From Cheshire, England, Dr. L. Golberg brought a report on the administration of 6,000,000 doses of iron dextran, a complex of ferric hydroxide and dextran. It is injected intramuscularly.

This compound causes neither immediate nor prolonged pain—a major drawback of the older parenteral preparations—and so far has not given rise to hemochromatosis.

Dr. Carl-Bertil Laurell of Malmo, Sweden, who has studied extensively the chemical aspects of iron utilized in clinical practice conceded that iron dextran is useful in some cases but advised against injections that yield a systemic net gain of more than 3 Gm. of iron. Hemochromatosis is a possible hazard. He cited the adverse effects of excess iron on the liver, the spleen, and the reticuloendothelial system in general.

Dr. Lynn A. J. Evans, an obstetrician from Charing Cross Hospital, London, told the symposium that many women are anemic to a degree before they become pregnant and that the condition is perpetuated by the childbearing. Thirty to 50 per cent of pregnant women cannot tolerate oral iron, he said.

The incidence of iron deficiency in pregnant women is five to 40 per cent. Most of them never recover from this condition because of blood loss during childbirth and subsequent pregnancies. It can result in dysmenorrhea, miscarriage, and other disorders. For anemic women, a small loss of blood is more serious than a greater one among normal females.

## New Rabies Vaccine

A new and safer rabies vaccine, produced in embryonated duck eggs, is now available to physicians and pharmacists. It has been shown in tests to be free of a "paralytic factor" that sometimes has caused paralysis and death during rabies treatment.

The new vaccine—an inactivated, or killed, virus vaccine—is being manufactured and marketed by Eli Lilly and Company. The result of six years of research and development work, it is the first commercially available vaccine for human use for which the rabies virus is grown in non-nervous tissue. The duck-embryo method was originated by H. M. Powell, Sc.D., of the Lilly biological research division.

The vaccine is "doubly safe" since the virus used in making it is of a strain which is nonvirulent in man. The nonvirulent virus is treated with a chemical which kills the virus but does not interfere with its antigenicity.

Local reactions to rabies vaccine of duck embryo origin have been observed to be somewhat less than those seen with vaccines of brain origin. Tenderness at the site of injection is common.

The new vaccine is more stable than that of brain origin, since the killed virus is packaged in dry form and mixed with sterile water just before use. This makes a longer dating period possible—eighteen months as compared to six months for unused vaccine of brain origin.

Rabies Vaccine, Dried Killed Virus (Duck Embryo), is sold in packages containing seven individual 1-cc. doses of dried killed virus along with seven ampoules of water for Injection, U.S.P. Two packages are required for a complete treatment which consists of subcutaneous administration of one dose each day for fourteen days.

## Oxypressin

Oxypressin (P. G. Katsoyannis, *J.A.C.S.* 79:109, 1957), a cyclic octapeptide amine containing a cyclic pentapeptide amide moiety identical with the one in vasopressin and a tripeptide amide side chain identical with the one in oxytocin, has been synthesized and tested for biological activity. It was found to possess oxytocic, avian depressor and pressor activities to quantitatively different degrees and in different ratios from those existing in oxytocin and vasopressin. This opens up the possibility of making chemical changes in natural hormones to produce synthetics with specific biological properties.

**Tetrex** (Bristol) is a new phosphate compound of tetracycline which is said to provide faster and higher tetracycline blood levels, practically double those obtained from tetracycline hydrochloride. It is available as capsules equivalent to 250 mg. tetracycline hydrochloride in bottles of 16 and 100 capsules.

**Antivert** (J. B. Roerig) is a two-colored elliptically shaped scored tablet preparation containing 12.5 mg. of meclizine hydrochloride and 50 mg. of nicotinic acid for anti-vertigo medication. It is available in bottles of 100.

**Supplifort Elixir** (White) contains two essential amino acids (lysine and methionine), eight important B vitamins, minerals and trace elements intended for use as a nutritional supplement. It is available in pint and gallon bottles.

**Enzeon** (Breon) is a suspension of 5,000 units of chymotrypsin in sesame oil, available in 5 cc. multidose vials.

**Clusivol Geriatric** (Ayerst) provides estrogen and androgen in small doses, along with vitamins, minerals and two amino acids. It is supplied as capsules in packages of 100 and 1000.

# ORAL Diabetic Drugs

(*Conclusion*)

*The first installment of his two-part article reported results of chemical and clinical studies of tolbutamide, a drug which can lower the level of blood sugar in diabetics. Discovered in Germany in 1954, tolbutamide is being produced by the Upjohn Company under the trade name Orinase.*

These results and others are interpreted by *W. E. Dulin and R. L. Johnston* to support the concept that Orinase stimulates the secretion of insulin or some other hypoglycemic agent by the B cells of the pancreas. It can, however, under certain conditions produce other actions which are probably not necessary for the hypoglycemic effect.

Hypoglycemic sulfonamides derived from thiodiazole or from urea have practically identical mechanisms of action, according to *A. L. Loubatieres.*

*In animals:* The presence of the pancreas is necessary for their action. Acute administration of the sulfonamide stimulates the beta cells of the islets of Langerhans, releasing a certain quantity of endogenous insulin. Large doses of sulfonamide potentiate the effects of exogenous insulin in the normal animal and in the depancreatized animal.

Chronic administration of sulfonamide tends to bring about the neoformation of beta cells and appears to cause and maintain the liberation of a larger quantity of insulin. Clinical trials show that diabetics can be grouped in three classifications: those who react to sulfonamides; those who show no reaction; those who benefit partially from treatment with sulfonamides. Favorable response seems to depend on the actual number of beta cells and amount of insulin in the pancreas. The action of sulfonamides on the liver is not yet completely known.

The use of sulfonamides in the treatment of diabetes mellitus requires caution because of the possibility that the beta cells may become exhausted in the case of certain diabetics, and because eventual sensitization or accumulation may occur in long-term treatment.

To elucidate the mechanism of action of sulfonylurea compounds extensive metabolic balance studies and numerous individual testing procedures have been performed before, during and following administration of Carbutamide and/or Tolbutamide by *S. S. Fajan et al.*

The data indicate that the sulfonylurea compounds (1) do not suppress the pituitary-adrenal system, (2) do not antagonize the peripheral effects of adrenal corticoids, (3) do not block the hyperglycemic effects of glucagon and adrenalin, (4) do not potentiate the activity of exogenous insulin, and (5) are not insulin substitutes. The blood-sugar lowering property of these compounds is via another mechanism.

Two patients with acromegaly and diabetes mellitus were placed on metabolic balance studies and given tolbutamide by *D. M. Bergenstal et al.* A third acromegalic patient without diabetes but with relative insulin resistance showed no alteration in glucose tolerance with administration of tolbutamide.

Two hypophysectomized and one adrenalectomized patient maintained on cortisone had similar glucose tolerance curves before and after tolbutamide. One adrenalectomized patient maintained on 300 mgm. cortisone daily developed steroid diabetes and did not respond to tolbutamide. A patient who had both adrenalectomy and hypophysectomy maintained on cortisone with a normal response to insulin showed equal glucose disappearance rates before and after administration of tolbutamide.

No definite conclusions regarding the mechanism of action of tolbutamide can be drawn from these observations. The pituitary gland does not seem to be necessary for the tolbutamide induced hypoglycemia. It does not seem that tolbutamide stimulates excessive amounts of insulin; however, the possibility exists that small amounts of insulin may be produced in response to tolbutamide for a prolonged period by the islet cells of the pancreas.

The prompt appearance of ketones in the urine upon the withdrawal of insulin is presented as a simple and rapid means of identifying patients who will not respond favorably to sulfonylurea therapy according to *G. G. Duncan.*

The clinician will not be entirely at ease in the use of sulfonylurea compounds until the exact mechanism of their function is know and proven to be innocent over long periods. However, with about 18 months experience with these products the favorable indications increase and, with suitable dosage, side effects are for practical purposes non-existent.

Clinical experience with BZ55 in 450 patients and with Orinase in 420 patients was reported by *A. Marble and R. Camerini-Davalos.* Of this number, 209 patients were maintained on BZ55 and 195 on Orinase for periods varying from two weeks to 14 months. Judged by strict criteria, 70 per cent of selected patients on BZ55 and 64 per cent of those on Orinase, achieved good or fair control of hyperglycemia and glycosuria. Untoward clinical effects were encountered in nine per cent of patients maintained on BZ55 and in 0.9 per cent on Orinase. The most common complication was a skin rash. No instance of leucopenia or agranulocytosis was encountered.

Jaundice developed in four patients receiving BZ55; one of these died. Liver function tests were made in 81 patients receiving BZ55 and similar studies are in progress in those who have received Orinase for long periods.

(*Continued on page 550*)

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# Compounder's Corner

## Alkylolamides

In cosmetics, the use of fatty acyl alkylolamides is by no means restricted to emulsification. They are indeed very versatile materials and many modern formulas for widely different types of cosmetics contain them. Probably the best-known non-emulsifying application is lipstick manufacture, where they form very effective non-volatile solvents for the halogenated fluoresceine dyes of the eosine type, as well as other skin-staining dyes. The use of alkylolamides for this purpose was discovered some years ago and is subject of a British patent, an American specification for which is pending. Indeed, the use of acyl alkylolamides as eosine solvents is widely known today. Another novel cosmetics application is in the formulation of face powder compacts, for which purposes some alkylolamides have just the right combination of characteristics.

The mono-alkylolamides are waxy materials, and on their own are substantially insoluble in water. The members of the class derived from lauric and myristic acids can, however, be soluble in water when they form part of a composition with other water soluble synthetic detergents.

These particular alkylolamides have the power of improving the soil removal efficiency of other detergents particularly sulfated and sulfonated detergents such as sodium lauryl sulfate or sodium dodecyl benzene sulfonate. They also have the power of enhancing the foaming powers of detergents.

Alkylolamides derived from higher fatty acids, are practically insoluble in water and do not improve the lathering power or soil removal efficiency of detergents, but they are valuable emulsifying agents, and in some cases they serve to render translucent detergent compositions opaque or pearly in appearance. It is also stated in the literature that certain alkylolamides derived from higher *unsaturated* fatty acids are useful as conditioning agents for the hair when incorporated in shampoos.

The di-alkylolamides are more soluble than those in the previous class. Until recently, the alkylolamides in this class were most frequently made not as the pure amide, but in the form of a complex composed of genuine amide, free amino-alcohol and some soap. There is considerable evidence that this complex does not function as a simple mixture and in this form many di-alkylolamides are readily soluble in water although they may be salted out by electrolytes under certain conditions. On account of their solubility in water, di-alkylolamides derived from lauric or myristic acid and diethanolamine in the form of the complex containing excess diethanolamine have found extensive application in the formulation of liquid detergent preparations. These alkylolamides have the power to augment the foaming power of other surface active agents under certain conditions and at the same time they have a thickening effect upon liquid detergent preparations generally. Unlike the products in class 1, which are purely effective as improvers for other detergents, the alkylolamides in this class possess, in the form of the complex, very considerable detergent power in their own right.

Until recently the di-alkylolamides have generally been available and used in the form of a complex. This was in many ways convenient, as the complexes were more soluble and possessed better wetting and detergent power than the pure amides, and also because it is simpler, and cheaper, to manufacture this type of product free fron undesirable by-products if an excess of alkylolamine is present. Where, however, these products are used in conjunction with sulfated detergents to enhance foam, the effective material is the true amide, while excess diethanolamine contained in the complex does not contribute.

In cases such as these, the di-alkylolamides can normally be adequately solubilized by the sulfated detergent and therefore the excess diethanolamine serves no useful purpose. Considerable publicity has recently been given to alkylolamides which are free from any large excess of diethanolamine. These materials have been widely described as "super-amides" or "extra-amides." They are weight for weight more effective for the purpose of stabilizing the foam of sulfated materials (or raising the viscosity of their solution), since they usually contain more than 90 per cent active amide.

Undoubtedly, there may be special purposes where free alkylolamine is definitely undesirable.

For the majority of applications, however, the whole issue would seem to hinge on the price for 100 per cent active amide in the nearly pure state as compared with the conventional "complex."

Where di-alkylolamide is being used as a detergent in its own right, alone or with only minor amounts of other detergents, the "complex" will be preferred on account of its all-round greater solubility and wetting and detergent power.

The products so far described, have been essentially nonionic in their behavior. It is possible by preparing the acid esters of sulfuric or phosphoric acid of these alkylolamides to produce detergents which are anionic in their behavior. In general, the monoalkylolamides are preferred for sulfation or phosphorylation. The sulfated monoalkylolamides of coconut oil fatty acids have ex-

cellent lathering power comparable with that possessed by sodium or triethanolamine lauryl sulfate. The show a superior detergency to the latter materials, and also greater ability when in dilute solution to retain dirt particles in suspension.

Probably the best known of this type of detergent is the sulfated monoethanolamide or isopropanolamide derived from coconut oil fatty acids. Detergents have been prepared from higher unsaturated fatty acids, and though under some conditions they lack the lathering power of the products from coconut oil, they do possess exceptionally good detergency and exceptional power to disperse lime soaps. Products containing as much as 50 per cent unsulfated material have excellent lathering and cleaning power.

Recently, there has been interest in the production of phosphoric esters of the alkylolamides. These have been claimed to have anti-static effect when used in the washing of synthetic fibers such as nylon. Other phosphoric acid esters of alkylolamides have found application in the production of a pearly effect in some types of cream shampoo.

Many compositions in practical use are improved by the presence of an alkylolamide. However, it is not always easy to measure this improvement quantitatively. One satisfactory way consists of devising a laboratory test which simulates the actual conditions under which a detergent product is to be used.

Many anionic detergents tend to lose their lather in the presence of oily and fatty soil and this effect is prevented by the use of suitable acyl alkylolamides. The effect is not quite true at all concentrations and the effectiveness of the alkylolamide only occurs above a certain threshold concentration of active detergent in solution.

The most used alkylolamides for the purpose of stabilizing foam are the monoalkylolamides and the di-alkylolamides derived from either lauric or myristic acid. Products derived from mixed fatty acids containing substantial proportions of lauric or myristic acids such as coconut oil or palm kernel fatty acids are also used. In general, however, it is generally found that the products derived from mixed fatty acids are only really effective in proportion to their content of lauric or myristic acids. The alkylolamides of the other fatty acids behave virtually as no more than inert diluents, although in the case of the monoalkylolamides products from mixed fatty acids sometimes have greater solubility in liquid detergent preparations. Therefore, it is frequently a better economic proposition to buy what is initially a more expensive product devised from a fractionated lauric acid than to use a mixed product which has a lower price.—K. R. Dutton and W. B. Reinisch, *Manuf. Chem.* Mar. 1957.

## International Cosmetics Symposium

R. Matalon in the *Manufacturing Chemist* for March 1957 provided a series of useful abstracts of papers given before the Second International Symposium of Synthetic and Natural Perfumes and Cosmetics in Paris.

A. Fayaud and S. Rivera discussed the utilization of fruit juices in combination with lipophilic adsorbable substances as hydrating and skin toning agents. By exposing certain Plants to low temperatures for several days, new materials called phytosatimulines are produced and these can be concentrated and may be used in cosmetics as growth stimulators in place of hormones.

H. Luzuy said that some pollen constituents might be useful in cosmetics. The water-soluble components and proteins are first extracted to remove allergens. The lipid residue, 5 to 15 per cent, contains fatty acids, cetyl alcohol, steroids, pigments, carotene and vitamins A, D, E and the B complex as well as vitamin B-7 (sic!) (Vitamin B-7 is not mentioned in standard references as part of the B complex).

N. Avalle discussed problems arising from instability when materials like hematopoietic serum, hydrolyzed keratin lactic ferments, turtle oil, etc. are used in cosmetic preparations.

F. Ardin reported on the use of lactic ferments in cosmetic preparations, sometimes with spectacular results; skin healing was said to be promoted in 24 hours after the application of these preparations.

## Calcium Gluconate Solutions

Studies on various solubilizing agents to make stable, soluble calcium gluconate solution for parenteral use were made by D. C. Chakravarty and J. W. Jones (*Drug Standards* 25:4, 1957). Three solubilizing agents, calcium lactobionate, calcium glucoheptonate and calcium levulinate, added in equivalent amount with calcium gluconate, produced stable solutions which do not develop a precipitate in the presence of solid particulates, changes in *p*H from 7.0, the presence of carbon dioxide or extreme variations in temperature.

Plain calcium gluconate solution, calcium gluconate solution in common use containing calcium *d*-saccharate and calcium gluconate solution containing ethylenediaminetetracetic acid, when placed in ampuls in the presence of sand and frozen, thawed and shaken for fifty-five minutes daily, showed an accelerated rate of precipitate formation.

The presence of carbon dioxide in the solutions of calcium gluconate studied did not appear to change the stability of the solutions.

Alterations of *p*H in all calcium gluconate solutions studied showed no appreciable effect on the stability of the solutions.

## New Insect Repellant

Diethyl toluamide, developed by the U. S. Department of Agriculture in cooperation with the Department of the Army, is said to be the best single insect repellant ever tested by these organizations. It can be used in contact with skin and clothing without harmful effect and protects against mosquitos, chiggers, flies and other biting insects.

The compound is both long last ing and potent, protection lasting as long as eight hours and it is especially active in repelling mosquitoes. As a component of an alcoholic lotion it leaves a pleasant-feeling deposit on the skin, free from stickiness.

Alhough the meta toluic acid derivative gives the most effective compound, the mixed isomers with about 75 per cent of the meta derivative are almost equally good. Hercules Powder Co. in making a technical grade of this material for use in formulations.

**Trilafon** (Schering), a phenothiazine derivative with the generic name of perphenazine is being offered for tranquilizer action. It is being made available as 2, 4, 8 and 16 mg. tablets.

**Suromate** (Patch) is a triple sulfa combination (100 mg. each of sulfadiazine, sulfamerazine and sulfacetimide) with 5.75 mg. of hyoscyamus extract and 200 mg. of potassium citrate. It is available in bottles of 100 and 500 tablets.

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# Skin Research

## Cosmetic Dermatoses

The term "cosmetic dermatitis" refers to an eruption that results from contact of the skin with a cosmetic preparation.

A dermatitis from cosmetics may be caused in one of three ways:

It may result from the direct chemical or physical irritation of normal, nonsensitized skin by an ingredient in the cosmetic. Such a primary cutaneous irritant causes a dermatitis by its action at the site of contact without the need for a previous sensitizing exposure. In sufficient concentration it will produce a dermatitis in practically anyone exposed to its action for a sufficient length of time. Also included here are greasy cosmetics, which may cause pustule formation by blocking the pilosebaceous apparatus or miliaria by plugging the sweat pores.

It may be caused by an otherwise harmless ingredient to which the skin becomes allergic. The true cutaneous sensitizer usually does not produce a dermatitis on initial contact but does so after an incubation period of a week or more. When this acquired allergic sensitivity has developed, the entire skin will be sensitive to the agent upon subsequent exposure.

It may result from contact with an ingredient that renders the skin locally hypersensitive to light of certain wavelengths. This is a so-called photosensitization dermatitis.

Most of the infrequent dermatoses caused by cosmetics today are due not to the direct irritant or the photosensitizing properties of the cosmetic but to the fact that the patient becomes allergic to one or more of its ingredients.

On the other hand, a primary irritant may also be a sensitizer. When an individual becomes allergic to a primary irritant, reexposure to a very small amount of the agent will cause a dermatitis, although similar untoward reactions are not produced in other persons with that particular concentration.

A primary irritant may cause a dermatitis on first exposure if it is permitted to act in sufficient concentration for a sufficient length of time. On the other hand, in the case of the true cutaneous sensitizer, only a certain percentage of those exposed will become sensitized and develop a dermatitis. Once a person becomes sensitized, however, subsequent contact with the allergen in the same or other areas of skin will cause a dermatitis.

When a primary irritant also acts as a sensitizer, concentrations of the irritant that are too weak to affect normal skin may cause a dermatitis in the allergic person. Patch tests of 0.1 per cent phenol on distant uninvolved areas of skin will give positive reactions in sensitized individuals but will cause no reaction in persons who are not allergic to this substance.

The use of cosmetics is a very old art. However, it was not until the present century, when the use of cosmetics by women of the so-called civilized countries became more or less universal, that untoward reactions to cosmetics in the form of a dermatitis became a well-recognized clinical entity. As is usual in sensitization phenomena of this sort, the number of individuals sensitized is proportional to some extent to the degree of exposure (i.e., the number at risk) as well as the sensitizing powers of the particular agents involved. For a long time dermatologists have recognized, studied, reported on, and treated these cases of cosmetic dermatitis. When sales in the cosmetic industry increased from 40 million dollars annually in 1914 to more than one billion dollars during recent years, the total number of cases of cosmetic dermatitis increased sufficiently to impress the physicians who were not dermatologists.

It is extremely difficult, however, to obtain accurate data on the incidence of cosmetic dermatitis or untoward reactions to the use of cosmetic agents. Apparently, in most instances, the patients will recognize and remove the cause of their cosmetic dermatitis before it becomes severe enough to require medical attention.

In any event, considering the ever-increasing use of cosmetics in recent years, the number of persons who develop dermatitis or other untoward reactions from their use is quite small. One must conclude, therefore, that the preparations available today are generally harmless.

Not only is the true over-all incidence of cosmetic dermatitis difficult to estimate, but it is also hard to obtain accurate data on the relative frequency with which different types of cosmetic preparations cause a dermatitis. At the present time, deodorants, depilatories, hair tonics and pomades, lipsticks, and nail polishes appear to be the more frequent causes of dermatitis due to cosmetics. Other cosmetics, of course, may also cause a dermatitis, but apparently they now do so relatively less often than do the aforementioned items.

The cutaneous eruptions caused by the use of cosmetics ordinarily have the characteristics of a contact dermatitis. Redness and edema, with the formation of papules and vesicles, are the rule, but more chronic changes, such as lichenification and hyperpigmentation, are rare. Usually the eruption is localized to the area of application of the cosmetic, but this is not always so. Sometimes the eruption appears at a distance from the site of application of the cosmetic, as, for example, in the case of dermatitis from nail polish.

The key to the diagnosis of a dermatitus due to cosmetics is the history of the patient. The appearance of the eruption, its localization, and clinical improvement after the discontinuance of the use of cosmetics are almost as important as the history in determining the diagnosis. The history is often difficult to elicit, and to do so may require some

time and effort. A woman and her cosmetics are not easily separated, and, although these patients do not mean to be dishonest, it is sometimes difficult to convince them that their cosmetics have played them false. Incidentally, when taking a history with the view to eliminating cosmetics, it is surprising how many patients do not consider wave set, shampoo, tooth paste, mouthwash, cologne, toilet water, and hand cream to be cosmetics.

Once the diagnosis has been determined, it may be confirmed by selective patch testing or, better still, by producing some recurrence of the dermatitis through limited reuse of the suspected cosmetic.

The patch test must never be used as a substitute for a good clinical history. A negative result means little, and, in actual practice, one may expect to confirm the diagnosis of a contact dermatitis in only about 30 to 35 per cent of cases through the use of such tests. In many cases the usage test will prove to be a more satisfactory procedure in confirming the clinical diagnosis of a cosmetic dermatitis.

If the key to the diagnosis of a cosmetic dermatitis is the history, the key to its treatment is avoidance. The treatment seldom presents a problem once the precipitating cause is removed. For this reason, the first step in therapy is the avoidance of all cosmetics of the type under syspicion. If there is doubt regarding the nature of the preparation responsible for the eruption, it is better to advocate complete elimination of all types of cosmetics for a while.

The use of simple wet compresses and calamine liniment or a bland emollient ointment will usually suffice for local therapy. When the eruption has subsided, the patient may be instructed to resume the use of cosmetics by reintroducing one item at a time at not shorter intervals than every fourth day. In this way the patient will not be deprived of all of these accoutrements. Should the dermatitis recur, the cosmetic item added last will probably be responsible —the recurrence thus tending to confirm the etiological diagnosis.—C. T. Nelson, *J.A.M.A.* 163:740, 1957.

## Skin Penetration by Sulfur

Sulfur, as shown by autoradiographic visualization by A. Scott (*Brit. J. Dermatol.* 69:39,1957) is able to penetrate readily through the normal epidermis. There appears to be no preferential site of absorption through the appendages.

$S^{35}$ shows an obvious difference in its pattern of behavior in the various dermatoses investigated. This alteration in site of localization and mode of distribution occurs in a predictable fashion for each type of disease and parallels, in its return to normal, the clinical improvement in the lesion.

On the basis of these tests there appears to be no abnormality, as far as the anatomical distribution of sulfur is concerned, in the uninvolved skin of the same patient or in the area of a previous lesion.

Sulfur is known to be present in two main chemical groups in the skin; in the molecules of chondroitin sulfuric acid and mucoitin sulfuric acid, components of the intercellular ground substance; and in the intracellular epidermal proteins, having disulfide or sulfydryl groups (e.g., methionine, cystine, and cysteine).

Microscopic examination of the autoradiographs in these experiments demonstrated that in the normal skin, and in the skin of lichenification, eczema, and discoid lupus erythematosus, the sulfur remained entirely extracellular, while in the cases of seborrhoeic dermatitis and psoriasis it became intracellular. Does this suggest that in the normal and miscellaneous groups the sulfur is absorbed through the intercellular substance of the skin, but that in seborrhoeic and psoriatic skin it becomes involved in an intracellular system containing sulfdryl and disulfide groups?

Finally, the striking tendency of $S^{35}$ to concentrate immediately deep to the midepidermis should be remarked. The location of the band thus formed is reminiscent of the so-called "keratogenous zone" of Giroud, which stains so densely with the Barrnet-Seligman stain for sulfydryl groups.

## Skin Penetration

At the Second International Symposium on Perfumes and Cosmetics (R. Matalon, *Manuf. Chem.*, March 1957), G. Valette discussed his latest studies in skin penetration. The substance is applied to the skin and the time required for contraction impulses in the leg is measured. Turpentine, oil of thyme and eucalyptus were found to be rapid penetrants. Ethyl alcohol is a poor penetrant alone but improves the penetration of eucalyptus and other substances able to dissolve in sebum, such as pinene, myrcene, linalyl acetate and geranyl acetate. The rate penetration decreases in the order of esters, alcohols, hydrocarbons.

## Psoriasis Treatment

NEW hope for victims of psoriasis, one of the oldest known and commonest diseases of the skin, is coming from a drug called Lipan.

Lipan is a defatted preparation taken from the pancreas of hogs and contains the fat-splitting enzyme lipase. It is reported either to remove completely the skin lesions caused by the disease or to keep them at a minimum, when it is used with a low fat diet.

Dr. Frank C. Combes, professor of dermatology and syphilology, New York University Post Graduate Medical School, New York, has been testing the drug for several years.

Dr. Combes believes that an important factor in the disease is faulty fat metabolism. He reported on a group of more than 100 patients in 65 per cent of these patients, Dr. Combes was able to get a "complete remission" of the lesions or keep them at a minimum.

This was accomplished by giving the patients Lipan capsules and keeping them on a low fat diet.

Lipan is being produced by Spirt & Company, Waterbury, Conn.

**Theradan** (Bristol-Myers) is an anti-dandruff preparation containing 3 per cent of Sarthionate-bis- (lauryltrimethylammonium) - polythionate-, 0.5 per cent tetradecylamine N-lauroyl sarcosine, both by weight, and 68.86 per cent by volume of ethyl alcohol. It is available in 5.5 ounce bottles in retailers' merchandising kits containing 24 regular cartons and two giant cartons of the product.

**Prednefrin Ophthalmic** (Allergan Corp.) for eye treatment contains prednisolone acetate 0.12 per cent, phenylephrine hydrochloride 0.12 per cent chlorobutanol 0.5 per cent sodium bisulfite 0.06 per cent, methylcellulose 0.12 per cent sodium borate 0.05 per cent sodium citrate 0.10 per cent; urea 0.05 per cent and aromatics 0.01 per cent in Ringers solution. It is available in 5 cc. "Drop Top" bottles.

**Leukeran** (Burroughs Wellcome) is a brand of chlorambucil, a nitrogen mustard derivative for the treatment of leukemia, lymphomas and Hodgkin's disease. It is available in 2 mg. sugar coated tablets in bottles of 50 tablets.

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(*Continued from page 449*)

Unfortunately these are the very areas where supplementation is most difficult. The economic barrier is a formidable one but even were it possible to surmount it such problems as distribution, overcoming local customs and changing cooking practices appear almost insoluble. Certainly the problems encountered in the rice enrichment program in the Philippines indicate that widespread adoption of any such program in underdeveloped areas is likely to be time consuming.

Recently Albanese[21,22] has reported that a high percentage of infants who fail to respond to conventional formulas grow normally after the addition of lysine to their diets. Holt,[7] on the other hand, reports investigations revealing the lysine requirement of the normal infant to be about 90 mg. per kilo of body weight, much less than is supplied in the average diets. While much additional data are required to confirm Albanese's observations it does not appear that the two findings are necessarily contradictory. It is possible that partial failure in digestion or absorption has linited the actual intake of lysine by the retared infants and that additional free lysine corrects this deficiency. This possibility becomes more credible in view of some interesting results obtained by Orten[23] in studying the absorption of amino acids from a blind intestinal loop in human subjects. She has observed that an equimolecular quantity of tryptophane greatly reduces the absorption of lysine. A child suffering from diarrhea might not retain its food long enough to allow sufficient absorption of lysine especially if one or more other amino acids are retarding its absorption.

## Animal Feeds

The diet of many farm animals consists largely of cereal grains and it might therefore be expected that lysine would prove an effective feed additive. However, as has been stated previously, soy bean oil meal is a good source of lysine. With the present price structure there is nothing to be gained by reducing the quantity of soy bean oil meal now commonly used in most rations. Even should a more nearly normal price relationship be established between corn and soy bean oil meal, a great deal of research remains to be done before it can be determined whether a diet consisting of corn, lysine and other food additives will be more economical than the mixed feeds now in use.

At present considerable quantities of animal by-products are incorporated into many manufactured feeds. These substances as a rule command a higher price than corn or soy bean oil meal. Should it be found that lysine can eliminate the need for such additives as fish meal, fish solubles, meat meal and tankage considerable saving might be effected. Recently it has been reported[24] that the protein level of turkey starter feed may be reduced from 28 to 20 per cent by replacing animal protein with 0.2 per cent lysine. Confirmation of these findings might create a considerable demand for lysine as a turkey feed additive.

The establishment of the place of amino acid supplementation in animal feed is a complex matter. Many factors such as the breeding of new animal and plant types are involved. It is probable that a clarification will not come for a good many years. One thing seems certain—widespread use of lysine as a feed supplement is not likely until the selling price has been reduced to within the range of one to three dollars per pound.

In some ways the preparation of lysine for animal consumption is less difficult than for human use. A concentrate containing lysine, arginine and histidine and small quantities of other amino acids might by simple ion exchange procedures be reclaimed from waste products which themselves are inedible. The presence of the other amino acids might actually be beneficial since even if not required as such, they undoubtedly would act as sources of non-specific nitrogen.

In a like manner if it should transpire that two pounds of DL-lysine could be synthesized more cheaply than one pound of the L-form, it would be entirely satisfactory to use the racemic form. There is no indication of toxicity of the D-isomer. In fact recent acute tests show the L-isomer to be the more toxic.[25] Evidence has also been presented to show that a portion of ingested D-lysine serves as a source of non-specific nitrogen.[26] In supplementation of human food in which taste, texture, color and bulk are much more important considerations it is possible that neither a lysine concentrate nor the racemic mixture will find as widespread use as the pure L-isomer.

## Amino Acids Imbalance

It has long been recognized that certain amino acids act as direct antimetabolites in microbial growth.[27] Amino acids balance in the diets of higher animals has received considerable attenti n especially after Grau[3] showed in 1948 that the lysine requirement of the chick is related to the protein level of the diet. This aspect of amino acids metabolism has been reviewed by Elvejhem and his associates[28,29,30] and it is the admirable work of the Wisconsin group which has contributed most heavily to the realization that amino acids imbalances may be more critical than was originally anticipated. Using weanling rats and diets containing 9 per cent casein they have shown interrelationships between many of the amino acids not only in effect on growth but also on percentage of fat in the liver. They have also carried out experiments in which amino acids have been added to diets containing only cereal grains as nitrogen

(*Continued on page 532*)

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# Perfumer's Shelf

## Flavor Symposium

Following the closing of the Flavoring Extract Manufacturers Annual Convention, The Society of Flavor Chemists plan a Luncheon and Flavor Symposium on Wednesday, May 22, 1957, at the Roosevelt Hotel, New York.

A unique and interesting program has been arranged for those who are interested in the subject of flavor. The program will include the following speakers: Dr. J. H. McGlumphy of Van Ameringen Haebler, Inc. on "Application of the Maillard Reaction in Development of Flavors;" Mr. J. Broderick, Lever Brothers Co., "Origin of Flavor;" Mr. Ernest Polak, Polak's Frutal Works, Inc., "Biosynthesis of Essential Oils."

A panel of flavor experts will be available to render expert advice on flavors for use in beverages, ice cream, candy, baked goods, spices, etc.

Representatives of the flavor and allied industries are invited to attend.

For further information and luncheon tickets, contact the Secretary of the Society of Flavor Chemists, Mr. Fred Schumm, Ungerer & Co., Inc., Totowa, N. J.

## Perfume Formulations

An experimental formula that can be used as a starting point in preparing rose bouquets is the following:

| | |
|---|---|
| Geraniol | 30 parts |
| Citronellol | 25 parts |
| Phenethyl alcohol | 25 parts |
| Linalol | 5 parts |

This skeleton formula can be varied and modified to suit a wide variety of requirements, as for example a superfine rose for extracts or cosmetics can be obtained by replacing citronellol by rhodinol, geraniol ex Java citronella by geraniol palmarosa, given added strength by traces of nonyl and lauryl aldehydes and tone by including geranium bourbon and alpha ionone and so forth. Interesting variations may be obtained by the inclusion of the esters (acetates, butyrates, etc.) of the rose alcohols—geraniol, rhodinol, citronellol and phenylethyl alcohol, and numerous others willl come to mind as the experiments proceed. Excellent fixation can be achieved by using phenylacetic acid, musk ketone, sandalwood and trichlormethyl phenyl carbinyl acetate in small quantities. The results obtained by the addition of 1-2 per cent of genuine otto or rose or a high grade imitation will easily justify the extra cost involved. For the less expensive soap perfume, special "soap" grades of the various aromatics are readily available and these together with a fairly generous percentage of diphenyl oxide and citronella oil Java or Ceylon will provide a good basis for further work.

Jasmin can be built upon the basic formula:

| | |
|---|---|
| Benzyl acetate | 40 parts |
| Linalol | 10 parts |
| Amyl cinnamic aldehyde | 15 parts |
| Cinnamyl alcohol | 5 parts |
| Phenethyl alcohol | 5 parts |

Numerous "build ups" of this basic formula will soon be found with a little experimentation, a fine sweet note is that most generally favored in Jasmin but various shadings towards fruity and rosy-lilac are also quite acceptable. A few suggestions for the elaboration of the above theme would include the addition of small quantities of other benzyl esters, in particular the butyrate and propionate, together with linalyl acetate or Bergamot oil to add a sweet freshness. Traces of methyl anthranilate and indole (not more than 1 per cent, generally less) may be used if desired but great care should be observed with a view to possible discoloration at a later stage. Once again a small percentage of natural jasmin or a good imitation will appreciably improve the composition providing the costs will permit. The sweet note can be further strengthened by the use of musk ketone as a fixative and a fruity background can be introduced by traces of aldehydes (so called) C.14 and C.16 in 10 per cent solution. Other products from which interesting modifications may be obtained include, hydroxy citronellal, ylang ylang, *p*-cresyl esters, sweet orange oil and many more. For soaps, good fixation is essential and the resinoids of styrax and benzoin will be found particularly useful.

Fougere perfumes are based on the powerful tones of oakmoss blended with the pleasing freshness of a lavender citrus complex and find appeal especially in the more masculine type of preparations.

| | |
|---|---|
| Oakmoss absolute | 4 parts |
| Bergamot oil | 15 parts |
| Lavender oil | 15 parts |
| Coumarin | 7 parts |

On the basis of the above formula depth of odor can be improved with the addition of 1-3 per cent of patchouly, vetivert and musk ambrette or ketone. For floral tones fairly liberal quantities of good quality rose and jasmin bases are recommended, with possibly a trace or orange blossom. Modifications of the fresh top note can be brought about by the use of such products as lemon oil, linalyl acetate or citronellyl formate and in certain cases, traces of tangerine oil. Many other materials may be used to provide varying creations, examples of these include geranium oil, clary sage, petitgrain, ylang ylang, sandalwood, amyl salicylate and ionone. Fixation is adequately taken care of by the basic ingredients already mentioned but if desired increased quantities of the musks along with vanillin may be incorporated. Cheaper versions and soap grades can easily be produced by using oakmoss resinoide and synthetic geranium and bergamot oils and by replacing the high priced lavender oil by lavandin.

Amber compounds provide not only popular perfumes in themselves but are also most useful for obtaining deep warm notes in almost all typesof fancy creations.

| | |
|---|---|
| Labdanum absolute | 10 parts |
| Musk ketone | 10 parts |
| Vanillin | 10 parts |
| Methyl ionone | 20 parts |
| Rose base | 10 parts |

The basic formula given above will be found most suitable for the heavier types but by alteration and substitution all tones will suggest themselves as experiments proceed. Lighter compositions will result from the use of bergamot oil, linalyl acetate or traces of lemon or tangerine oil together with an increased quantity of the rose base or such rose alcohols as rhodinol, geraniol or phenylethyl alcohol. If the finished compound is required as a base and a semi solid substance is acceptable, then the deeper tones could be considerably strengthened by further quantities of musk and vanillin, plus a fairly heavy percentage of coumarin, benzyl *iso* eugenol, vetivenol and sandalwood. A liquid product can be obtained by adding quite large quantities of 3 percent tincture of musk, civet or castoreum. For a variety of interesting compositions experiments with the following are recommended, oil of Peru balsam, clary sage and oakmoss, also some of the many amber type specialities readily available on the market today.—L. M. Stringfellow, *Chem. Prod.* 20:67, 1957.

A really good violet perfume is not easy to compound, but many interesting shades are possible and the following formula will provide a good starting point:

| | |
|---|---|
| Methyl ionone | 30 parts |
| Alpha ionone | 15 parts |
| Bergamot | 10 parts |
| Heliotropin | 4 parts |
| Methyl heptin carbonate | 0.5 parts |

formula will provide a good starting point. If cost is of primary importance ordinary ionone 100 per cent may be used, together with a good synthetic bergamot either as an extender or a complete replacement for the natural oil. To obtain a sweet floral background about 3-5 per cent of ylang ylang oil and smaller amounts of the natural absolutes of cassie, mimosa, jasmin and violet leaves will be most beneficial. Again, if cost prohibits the inclusion of these costly natural materials, many excellent specialty replacements are available and can be used to great advantage. For cheaper versions use may be made of such aromatics as anisic aldehyde, benzyl acetate, terpineo and its esters, phenylethyl alcohol and esters, also traces of lauryl aldehyde in 10 per cent solution. Fixation will largely be taken care of by the natural absolutes but in their absence and also to supplement them, about 1-5 per cent of sandalwood, orris resinoide, musk ambrette and ketone, or vanillin will prove of value. Violet soap perfumes may contain cananga synthetic in place of ylang ylang, "soap" grades of the ionones along with fairly generous quantities of the resinoides of benzoin, Peru balsam and styrax also musk xylol and sandalwood and vetivert residues.

The perfume of lily of the valley is probably the most exquisite of all the florals and care should be taken to produce a compound which in dilution is both delicate and elusive but yet at the same time sweet and persistent.

| | |
|---|---|
| Hydroxycitronellal | 30 parts |
| Linalol | 15 parts |
| Terpineol | 15 parts |
| Rhodinol | 10 parts |

Experiments may proceed on the basis of the above, blended with such products as ylang ylang, phenylethyl alcohol, geranyl and citronellyl esters, bergamot and benzyl acetate in relatively small proportions. Traces of phenylacetaldehyde dimethyl acetal are particularly useful for obtaining a green freshness, but this must not be taken to excess, 1 per cent of a 10 per cent solution being considered ample. The floral note can be further strengthened with good rose and jasmin bases and minute traces of cyclamen aldehyde. As fixatives use can be made of musk ketone, methyl naphthyl ketone and trichlormethyl phenyl carbinyl acetate. In the case of cheaper compounds and perfumes for toilet soaps, bois de rose oil may be used to replace linalol, together with "soap" grades of hydroxycitronellal, phenylethyl alcohol and so forth.

## Piquancy

It is the merging of the slightly Oriental type of spicy undertone with the floral nuance which is responsible for some very intriguing effects in bouquets. Nevertheless, it is a fairly common experience that carefully compiled formulas for plain and fancy carnation compounds sometimes turn out disappointingly dull and lifeless. Such efforts seem entirely lacking in the piquancy which to a large extent constitutes the charm of the living blossom scent, and although by carefully shading such a compound with traces of black pepper oil, certain mint oils, and methylhexyl or similar ketones, a certain degree of pleasant pungency can be conferred, this procedure is a somewhat mechanical titillative measure and not a true source of this somewhat elusive enlivening adjunct.

The spicy radicals conveniently align into complementary pairs, for example almond–vanilla, cachou–nutmeg, and in the case of the clove, cinnamon seems to be the ideal counterpart. In the same way in which the dividing line between Spices and Condiments is indefinite, it may be remarked that the many natural osmical interweavings of benzoic and cinnamic alcohols, acids, aldehydes and esters, are common to the Balsamic as well as the Spicy sectors. By sundry tabular arrangements under these headings, the basic elements (for example those comprising a Spicy-Vanilla) can be compared with the alternatives, which in this case constitute a Balsamic-Vanilla, both of which are very common components in the make-up of tropical blossom fragrances.

This digression affords some insight into the technique employed in the examination of the scent of living blossoms, whereby certain parts, as it were, are dissected and set aside for further consideration. Thus, in the case of the Carnation, we know that the eugenols provide the foundation, but the elusive element of spicy piquancy calls for a more detailed consideration.

Attention is now directed to the complementary cinnamon-type nuance. This is not, however, to be found in the somewhat harsh-odored cinnamon or cassia oil aldehydes, but in the soft, sweet and mellow combination of alkyl cinnamates with cinnamic alcohol. It may be remarked in many instances—as among the blossoms of the Myrtle and Allspice trees—that the presence of eugenol is invariably accompanied by cineole and bornyl acetate and essential oils from these sources frequently exhibit albeit somewhat crudely, a merging of pungency and piquancy.

It is instructive in practical work to note the gradual development of piquancy which follows upon the addition to a eugenol base of terpeneless spike, lavender or rosemary, a little vanilla and a trace of a cinnamyl complex. —E. S. Maurer, *S. P. C.* 30:317, 1957

# Industry's Books . . .

**Hormones, Brain Function, And Behavior,** *Edited by Hudson Hoagland, The Worcester Foundation for Experimental Biology, 257 pp., Academic Press Inc., New York, (1957), cloth,* **$7.**

This book constitutes the report of a conference on neuroendocrinology held in May, 1956, at Columbia University's Arden House on the Hudson. Twelve papers were presented on aspects of neuroendocrinology during the two-day meetings. The papers and discussions of this symposium are aimed at elucidating selected aspects of hormone actions in relation to brain function and behavior.

**The Adrenal Cortex,** *by I. Chester Jones, Department of Zoology, Univeristy of Liverpool, 316 pp., New York: Cambridge University Press,* (1957), *cloth,* **$7.**

The adrenal glands in animals are normally situated near the kidneys, and one of their functions is the secretion of hormones. The inner part, the medulla, produces adrenaline, and the surrounding tissue, the adrenal cortex, produces substances related to cortisone, which is used in the relief of rheumatoid arthritis and other diseases. Alterations in the secretions are connected with some types of high blood pressure; and, in general, the various products of the adrenal cortex play an essential part in the functioning of living creatures. It has long been a major subject of study by endocrinologists. This monograph is the first to give a comprehensive account of the workings of the adrenal cortex in all the various biological species among the vertebrates.

**Practical Dermatology,** *by Samuel M. Peck, B.S., M.D., Dermatologist to the Mount Sinai Hospital, and Laurence L. Palitz, M.D., Ph.D., Long Island Jewish Hospital, 380 pp., Illus., Landsberger Medical Books, Inc., New York, (1956), cloth,* **$7.**

This is a survey of dermatologic disorders as they are commonly met with in daily practice. The authors then proceed to a complete discussion of each disease—its etiology, pathologic-physiology and therapy. Because of the recent introduction of many new and potent therapeutic agents in the field of dermatology, the general physician will find this volume especially timely and of immediate use in his daily practice.

**An Outline of Bacteriology And Immunity,** *by Ronald Hare, M.D., Professor of Bacteriology in the University of London, 418 pp., Longmans, Green And Co., New York, (1956), cloth,* **$7.**

This text book is founded on the lectures given by the author to students at a London medical school and incorporates what is increasingly becoming the practice in the teaching of bacteriology and immunity to medical students. Viruses and fungi are therefore given weight equal to that accorded to the bacteria, while the principal emphasis is laid rather on the fundamental principles involved in the relationship between micro-organisms and Man than on the minutiae of bacteriological technique or the cultural and other characteristics of microbes. Detailed attention is given to such aspects of the subject as the growth of micro-organisms, the agencies that are harmful to them and the part the latter play in the sterilization of materials used in medicine; the mode of action of chemotherapeutic drugs and the resistance which organisms may acquire are also discussed. Much attention is devoted to the importance of endemic and epidemic infection both to the individual and the community and a whole chapter is devoted to a discussion of the sources and modes of spread of pathogenic micro-organisms.

**Drugs In Current Use 1957,** *Edited by Walter Modell, M.D., F.A.C.P., Cornell University, 152 pp., Springer Publishing Co., New York, paper binding,* **$2.**

This is the third, annually revised alphabetical listing of drugs in common use. The purpose is to provide a concise statement of the principal pharmacologic characteristics of drugs in current use; major uses; physical properties; absorption; actions, both therapeutic and toxic; mode of administration; preparations; dosage; specific antidotes against poisoning when these are available. It is a capsule-account of the data essential to the sensible exploitation and safe handling of a drug.

**The Pharmaceutical Industry,** *by John O'Neil Closs, Revised Ed. 1956, 28 pp., Bellman Publishing Co., Cambridge, paper binding,* **$1.**

This deals with the pharmaceutical industry and is one of a series in the vocation and professional monograph series. The pamphlet includes—History of the occupation or industry—Qualifications for employment—Training required—Methods of entry—Opportunities for advancement—Earnings—General Trends in the occupation or industry. Sources of further information.

**Dorland's Illustrated Medical Dictionary, 23rd. Ed., Including Modern Drugs And Dosage,** *by Austin Smith, C.M., M.D., Editor Journal of the American Medical Association, and Fundamentals of Medical Etymology, by Lloyd W. Daly, A.M., Ph.D., Associate Professor of Classical Studies, University of Pennsylvania, 1598 pp., W. B. Saunders Co., Phila., (1957), flexible binding,* **$12.50.**

The increasingly rapid expansion of medical research and knowledge, in the closing half of the 20th century, has brought its inevitable increase in the vocabulary, which is reflected in these pages with the addition of thousands of new terms. Besides the addition of new terms, tens of thousands of definitions have been scrutinized and thousands have been rewritten to conform with changing concepts or expanded knowledge. The entire history of The American Illustrated Medical Dictionary, since the first edition appeared in 1900, has been one of steady growth, in usefulness as well as in size. Consultants and Major Contributors to this work are too numerous to mention here.

**Handbook Of Solvents, Vol. 1 Pure Hydrocarbons,** *by Iberl Mellan, Director of Research and Production Pioneer Chemical Co., Inc., 249 pp., Reinhold Publishing Corp., New York, (1957), cloth,* **$6.50.**

To be published in several volumes, this reference work presents concise information on the composition and properties of industrial solvents. This initial volume is devoted to pure hydrocarbons of all types—aliphatics, aromatics, and terpenes. Commercial and proprietary names are used in lieu of chemical nomenclature; the hydrocarbon solvents are classified in accordance with their distillation range; and wide spectrum of properties is given in tabular form for each solvent.

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(*Continued from page 526*)

sources. For instance it was found that an unsupplemented rice diet gave very poor growth and a very high liver fat. The inclusion of 0.2 per cent L-lysine hydrochloride and 0.24 per cent of DL-threonine produced a very significant increase in growth rate but had no effect on liver fat. Increasing the lysine supplement to 0.4 per cent reduced the liver fat to normal but also caused a reduction in growth rate which again could be overcome by increasing the levels of leucine, isoleucine, valine and histidine.

It is difficult to over estimate the importance of these findings. They emphasize the very complex relationship that exists among all metabolites and just how much remains to be done. On the other hand the existence of amino acids imbalance should not preclude judicial food supplementation. On the contrary just the opposite is indicated. It should be remembered that the unsupplemented rice diet produced a high liver fat. Thus amino acids imbalance can and undoubtedly does exist in nature. What is more logical than to correct it when possible?

On the basis of Elvejhem's work it has been suggested[7] that lysine supplementation of infant formulas is a dangerous practice. Granting that the benefits claimed to be derived therefrom need confirmation, it seems unlikely that harmful effects will be encountered from discriminating supplementation. It should be remembered that most if not all of the effects observed with variations of one hundred per cent or less of any single amino acid have occurred when the protein intake was low. With a high protein diet such as is consumed in the United States, the chances that reasonable variation of any of the amino acids will be harmful appear to be remote. Recently a grossly unbalanced amino acids mixture has proved effective in the treatment of an inherited metabolic disease, phenylketonuria. Other abnormal conditions may yield to similar treatments. It is within the realm of possibility that the retarded infants studied by Albanese fall in such a category.

Single injections of 5 grams of lysine in adults have been found to increase the urinary excretion of cystine, arginine and ornithine.[31] The blood levels obtained when so large a quantity of lysine is injected are undoubtedly many times those which exist during oral absorption. Since tubular reabsorption of amino acids is known to be a competitive mechanism, it is not surprising that under these abnormal conditions the excretion of other amino acids is increased. The possibility that such increases are indicative of toxic effects of rational supplementation, as recently suggested,[7] seem remote indeed.

## Summary

In conclusion it may be said that the potential for lysine supplementation of human food and animal feeds is great. Just how much of this potential will eventually be realized is not now known nor is it likely to be known for many years. Careful Supplementation especially of cereal products, can be undertaken without fear of deleterious effects. The keynote for amino acids supplementation has recently been sounded by the Food and Nutrition Board of the National Research Council. This body recognizes the potential value of proper supplementation but emphasizes the need for intensive study of the problem. Certainly this is a progressive attitude and one to be applauded.

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## EYE MAKE-UP

(*Continued from page 451*)

trial and error judgment.

Eyebrow pencils are most commonly made in the regular pencil form. Their manufacture, therefore, now has been taken over by the major lead-pencil manufacturers, with very few exceptions. This came about because pencil manufacturers already had the manufacturing equipment—particularly for embodying the vehicle in its cylindrical wooden container. Formula changes, of course, had to be made from the regular writing pencil formula—but this was easily accomplished. Since the market for items of this sort is small, there is no great emphasis on methods of development of a probably better product. There are, however, some eyebrow pencils still made by cosmetic producers. They consist of a vehicle which is a rather hard pomade into which the color is ground and then remelted and poured into molds. A typical formula would contain mineral oil, and waxes particularly some carnauba to impart sufficient rigidity.

(*Continued on page 534*)

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(*Continued from page 532*)

Eye shadows are made by grinding the colors into a suitable base. The vehicle used varies but a mixture of mineral oil petrolatum and a wax is satisfactory. The color concentration varies with the color used and some titanium oxide or zinc oxide is also used to effect the proper opacity. The average pigment concentration including the titanium oxide would usually be about 20 per cent but could run as high as 35 per cent. The color usually used to provide a black shade is either ivory, bone or lamp black—a grey shade will consist of a mixture of ultramarine blue and titanium oxide or carbon black and titanium oxide or a mixture of all three—blue is provided by ultramarine blue. The use of chrome oxide is thought to be somewhat hazardous and the greens for eye-shadow are, therefore made ultramarine blue plus an ocher which would give the appropriate green.

Browns are provided by a mixture of siennas and umbers or by red oxides and umbers. These colors are relatively drab as compared to lakes but as the name—"shadows"—they are supposed to be subdued.

In manufacture the base is melted together with the pigments and filler added and the whole ground through an ointment or roller mill. The ground mass is then remelted and poured into the containers.

This article covers a small but important segment of cosmetic make-up preparations. The descriptions by their very nature must be generalized, but I think the methods by which the formulater may arrive at any desired result are considered.

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## TIME-INTENSITY STUDIES

(*Continued from page 453*)

A third application of this type of study, this one not dependent upon bitterness, is to help describe the flavor of chewing gum. Flavorants in gum should be quite obvious and should have suitable lasting power.

For purposes of standardizing these time intensity measurements, each panel member used one stick of gum and chewed at a rate of approximately 50 chews per minute.

The flavor develops quickly, one minute after chewing has begun the flavor has reached a moderate level, and it maintains this level for a period of two minutes. Gradually the intensity of the peppermint decreases, but it remains at a slight level for approximately four minutes more (see the 5 to 9 minute periods in Fig. 4.). By the end of ten minutes the flavor is just barely perceptible, and at the end of eleven minutes has disappeared.

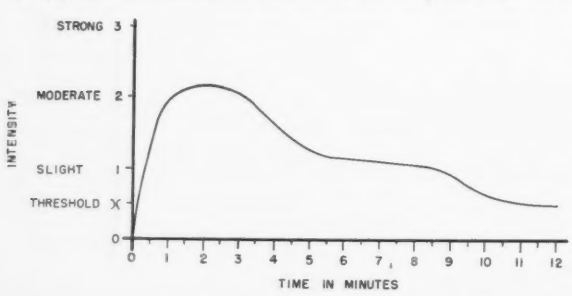


FIG. 4 FLAVOR CURVE OF PEPPERMINT CHEWING GUM

This diagrammatic relationship between the strength and the duration of the peppermint characteristic points out where the use of time-intensity curves can be most beneficial. In this instance several different peppermint formulations would be tried and time-intensity curves established for each formulation. Valuable information will thus be gained leading to the choice of the most successful flavorant material.

Time-intensity curves very seldom give a final answer to a flavor problem. However, they are one more tool for the flavor chemist to use, and as such can be relied upon to give guide posts to good and lasting flavor.

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## HYPERTENSION DRUGS

(*Continued from page 455*)

### Hexamethonium

(Hexamethylene bis (trimethyl ammonium chloride)

Hexamethonium was the first effective ganglion blocker developed and is still widely used. Unfortunately, the oral dose to parenteral dose varies widely, often as much as 100 to 1. Erratic absorption from the gastrointestinal tract when given orally makes parenteral administration preferable in many instances.

Despite the drawbacks, successful oral therapy is frequently obtained if carefully regulated doses are given and the patient given careful attention. The combination of hexamethonium with hydralazine appears capable of controlling even the most severe hypertension.

Toxic reactions to hexamethonium include dryness of the mouth, severe constipation, inability to empty the bladder, and blurring of vision. When high dosages are used there are rare cases of pulmonary fibrosis.

### Pentolinium (Ansolysen)

Pentamethylene 1,5 bis (1' mythyl pyrrolidinium bitartrate

Pentolinium (Ansolysen; Wyeth) followed soon after hexamethonium. Though possessing material advantages, the claim of greater predictability of effect has not been conclusively proved. Ansolysen has a better oral-parenteral ratio than hexamethonium, exerts a slightly longer effect and is probably somewhat less toxic. There is less constipating effect, especially after the first weeks, and as yet no pulmonary changes have been reported. The dose is about a fifth that of hexamethonium, with

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less tendency to produce severe hypotension.

While pentolinium is undoubtedly a valuable addition there is little doubt that early claims and hopes have not been fully realized. Practically all the side effects of hexanethonium in varying degree are noted.

### Chlorisondamine (Ecolid)

β-ethyl (1-methyl 4,5,6,7, tetrachloro indolinium trimethyl Ammonium Chloride)

Chlorisondamine (Ecolid; Ciba), the most recent entry into the autonomic blocking field is similar to pentolinium in effect but possesses a longer duration of action and a greater predictability than the previous two ganglion blockers. Less fluctuations in blood pressures and lowered parasympathetic side effects are claimed. Unfortunately the same undesirable side effects as the other ganglion blockers, particularly in visual blurring, are obtained. Faintness, dizziness and weakness may occur. However, the long acting properties of the drug are attracting considerable attention. A dose given once in twelve hours is usually sufficient to bring about good control in all but the most severe hypertensive patients.

For parenteral control, pentolinium or chlorisondamine are the drugs of choice. The duration of action may be anywhere from fifteen minutes to fourteen hours. For ambulatory patients chlorisondamine and mecamylamine are preferred because of better predictability.

### Mecamylamine (Inversine)

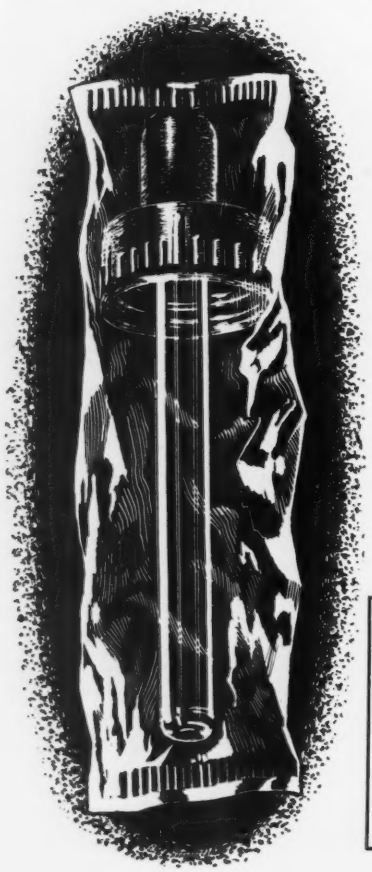
Mecamylamine (Inversine; Merck Sharp & Dohme) is considered the drug of choice by many specialists in moderate to severe hypertension, due to the long duration of action (17 hours average) and prompt onset (usually about oue hour) and especially due to its complete absorption when administered orally. Blood pressure fluctuation is smoother and more predictable than the ganglion blockers. The therapeutically necessary dose is the smallest of all the ganglionic blockers. Mecamylamine appears to be 10 to 20 times more potent than pentolinium and about 90 times more potent than hexamethonium. However, parasympathetic side-effects are just as prominent with these small doses as with larger doses of other agents. The major side effects are urine retention and intestinal paralysis. The minor ones include loss of visual accommodation, dryness of mucous membranes and diminution of normal sweating.

A major point in favor of Inversine is the near unity of the effective oral and parenteral dose as contrasted with the average 10 to 1 ratios for the other ganglion blockers.

Combinations of Rauwolfia and mecamylamine give more satisfactory responses than with the latter alone. There is less blockade of the parasympathetic nervous system with reduced severity of side effects.

Research continues at a hightened pace in the

*(Continued from page 540)*

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# Trade Literature

### Hexachlorophene USP-30

Sindar Corporation, 330 West 42 Street, New York 36, has published a supplement to its Technical Bulletin H-1 entitled G-11 (hexachlorophene USP) An Annotated Bibliography. The supplemental bibliography appears in the Sindar Reporter No. 1-1957, and includes abstracts of 28 articles and 1 patent.

### Rauwolfia and its Alkaloids

S. B. Penick & Company, 50 Church Street, New York 8, has issued a supplement to the bibliography which it issued in September, 1956 on Rauwolfia and its alkaloids.

### Cellophane-Handling Posters

American Viscose Corporation, 1617 Pennsylvania Boulevard., Philadelphia 3, have available posters presenting the rules for proper storage and handling of cellophane. Designed for hanging in the storage and wrapping areas of packaging plants, the two 17″ by 22″ posters are printed in black and green.

### Aerosol Emulsifier

Emulsol Chemical Corporation, 75 East Wacker Drive, Chicago 1, has issued Technical Bulletin No. 49, entitled Application of Emcol 14 as Emulsifier in Aerosol Emulsions. It is claimed that many more products can now be aerosol-packaged because of the availability of this emulsifier. Used with fluorinated hydrocarbon propellents, the emulsifier creates desirable sprays with minimum foaming and container corrosion. It also assures a satisfactory sprayable emulsion system containing water-soluble products.

### Standard Aromatics Bulletin

Standard Aromatics, Inc., 88 University Place, New York 3, has introduced a bulletin devoted to periodic reports "on timely developments, news and views, for the perfume arts and sciences." The first bulletin, dated April 1957, discusses perfumes for thioglycolate solutions, unusual fragrances (flavors employed for perfume purposes), the perfuming of iodophors, and a roundup of aerosol tips.

### Liquid Processing Equipment

Alsop Engineering Corporation, 1200 Winner Street, Milldale, Conn., has issued a new 40-page Liquid Processing Equipment Catalog, No. G-956. Written especially for plant personnel, the catalog contains photographs, diagrams (some full page size), and comprehensive information on the entire line of stainless steel liquid processing equipment, including filters, fixed-side and top-entering agitators and transfer pumps. Each product is treated separately, features are described clearly and completely with an explanatory text, numerous plant installation illustrations, design variations, detail drawings and parts lists, application and performance data.

### Guar Gums

A new 16-page booklet on Jaguar, a complete line of uniquely processed guar gums, has been issued by Stein Hall & Co., 285 Madison Avenue, New York 17. The brochure describes in detail the unusual combination of physical and chemical properties possessed by this pure vegetable colloid. It also gives information on food and drug standards on guar gum, handling methods, types available, applications, etc.


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# Readers' Questions . . .

**Bitter Cough Syrup:** *We have a cough syrup based upon codeine, an antihistamine, ephedrine, belladonna and aconite which is very bitter and we would like to be able to prepare this to be palatable to children and adults. We would appreciate your suggestions in this matter.* VENEZUELA.

Each bitter Pharmaceutical preparation is an individual problem in flavoring and only the most general advice can be given you; you ought to be able to obtain valuable information from your regular flavor supplier. Bitterness is dependent not only upon the presence of bitter principles in the mixture, but also upon their concentration and the amount administered in a single dose. Much can be done as a starter to cover the bitter taste by making the mixture quite sweet by the addition of sugar and glycerin; synthetic sweeteners are also useful but must be used cautiously, since excess will add to the bitterness. Finally, in our own experience, the licorice flavor is very useful in covering bitterness. This flavor is unfortunately not universally acceptable so that after licorice has been used to mask the bitterness it may be advisable to add another flavor pomponent as a modifier.

**Nail Poilish Remover:** *We use two formulas for nail polish removers and would appreciate information from you concerning possible improved formulas and ingredients.* ARIZONA.

You did not mention ethyl acetate as an ingredient you now use; this is not new but it is popular and effective. Some of the glycol ethers used as lacquer solvents may be useful to you since they are good polish removers but have an odor that is easily covered. Twenty to thirty per cent of deodorized kerosene or similar hydrocarbon solvent may be added to the solvent mixture without adversely affecting the ability to remove polish and lanolin derivatives and vegetable oils may be used in small proportion to make an "oily" polish remover.

**Aerated Tooth Paste:** *The tooth paste we prepare has much air incorporated in it and we would appreciate any suggestions you may have to offer to remove this air.* BRAZIL.

About the only feasible suggestion that can be given you is to change your

equipment and method of manufacture to keep the air out of your tooth paste in the first place. The customary method of removing air from non-volatile mixtures, by keeping the preparation under reduced pressure while stirring, would not be especially effective for a thick paste.

**Thin Hand Lotion:** *The hand lotion I make according to the inclosed formula is heavy when first made but in a few days becomes very thin. How can I prevent this lotion from becoming thin.* CHICAGO.

You can't. The thickness is an illusion, because at equilibruim, reached only after a few days' standing, the mixture will be naturally thin. This is the case where the emulsion contains little oil or other emulsifiable components. You should be able to improve your lotion considerably by replacing one-fourth to one-half of the stearic acid with an emulsifying grade of glyceryl monostearate.

**Universal Indicator:** *Can you give me a formula for an indicator or indicator mixture that will change to a series of different colors according to the pH value.* NEW YORK.

The Merck Index gives the following directions for preparing an universal indicator: dissolve 60 mg. methyl yellow, 40 mg. methyl red, 80 mg. bromthymol blue, 100 mg. thymol blue and 20 mg. phenolphthalein in 100 cc. of ethyl alcohol and add enough 0.1 N sodium hydroxide solution to produce a yellow color. This indicator changes color from cherry-red at pH 1 through orange-red at pH 4, yellow at pH 6, green at pH 8 to blue at pH 10.

**Cloudy Cologne:** *The cologne I make by dissolving 6 per cent of the perfume oil in 60 per aqueous alcohol is still somewhat turbid after being filtered through filter paper and becomes even cloudier on standing. Can you suggest how I may overcome this difficulty.* SAN FRANCISCO.

Several things are possibly wrong: you may be trying to dissolve more oil in the alcohol than it can take; the alcohol may be too dilute; filtration may be less effective than you think. Corrections following from these possiblities are to use somewhat less of the oil or increase the proportion of alcohol if you can see actual undissolved droplets. Then, to remove and prevent the recurrence of turbidity, the mixture should be chilled overnight to 45°F., and then filtered cold with the help of talc or another filter aid.


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(*Continued from page 536*)

field of ganglionic blockers, especially for a drug with lessened toxic effects.

### Veratrum

The Veratrum alkaloids were heralded as a great hypotensive break-through when they appeared some years back. Unfortunately they do not appear to have lived up to original expectations.

Their principal clinical use is in acute hypertensive crises, reducing the blood pressure to normal irrespective of the primary cause. Tolerance to dosage appears rapidly and continuous normotension is difficult to achieve. Although the veratrum drugs are capable of a broad attack on the hypotensive problem, the narrow dosage range between effective levels and those causing nausea and vomiting render the drugs somewhat impractical. There is usually less nausea if veratrum is given with Rauwolfia.

The preparation of a mixture of pure crystalline protoveratrine A and B from veratrum album has resulted in a drug of greater potency, but it too is limited by a narrow toxic to therapeutic action.

Work on veratrum derivatives is continuing. Synthetic derivatives are being prepared, all with an eye to widening the therapeutic ratio.

### Miscellaneous

A potentially very fruitful attack on the hypertensive problem utilizes the antimetabolite point of view. This is principally the work of D. W. Wooley and E. N. Shaw at the Rockefeller Institute. Since serotonin has been shown to be a pressor chemical, a search for antagonists was initiated. 1-Benzyl-2, 5-dimethyl serotonin has shown promise in preliminary clinical treatment.

The adrenergic blocking agents are used as diagnostic aids and to overcome vasoconstriction in peripheral vascular disease. They are rarely, if ever used routinely in the treatment of hypertension.

Some of the "stand by" drugs continue to be used in the treatment of hypertension: the barbiturates for their calming effect and the nitrates—mannitol hexanitrate and erythritol tetranitrate—for their vasodilating effect. Potassium thiocyanate is still of some value in treating hypertensives with intractable headaches, but in general it is too toxic for long use or for practical long term management. The drug has been superseded.

The dihydrogenated ergot alkaloids, dihydroergocristine, dihydroergocornine and dihydroergokryptine have been widely used in Europe as hypotensive agents. They stimulate directly the plain muscle of blood vessels. However in acceptable doses, they do not often maintain adequate blood pressure falls.

### Research Future

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hypertension? No, since patients respond so differently there must be periods of trial to discover individual treatments.

The future of research according to Dr. Page, must be concerned with clinical conditions which seem inseparable from hypertension, such as atheriosclerosis. Many patients' blood pressure become well-controlled but atherosclerosis develops. What is needed is a drug that will keep pressures lowered and also stop atherosclerosis. Whether renal arteriosclerosis precedes hypertension or vice versa is a focal question. Blocking agents must be improved. Especially needed are drugs that will act primarily on peripheral circulation, without the side effects of adrenergic blocking agents.

The surface has hardly been scratched as to the causes of high blood pressure. Whether essential hypertension is a disease entity at all or a complex of many arising from numerous causes is a basic question. The diversity of current remedies for hypertension and the disparity in their effect (reducing blood pressure in some cases but not in others) seems to indicate that "essential" hypertension is not one disease but many diseases having nothing more in common than the elevation of blood pressure. Answers to the questions whether involvement of the kidneys plays a part in the origin of hypertension is still inconclusive.

The degree to which psychic and emotional factors cause hypertension is giving way to precise investigation. However, various reports of prolonged psychotherapy have not indicated any cures of hypertension. The patient may be better adjusted, blood pressure may be a little lower but the disease is still there. These are only a few of the myriad of questions.

It is obvious that medical scientists are aware of the problems. With their findings should come the guideways for the synthetic organic chemist to plan more specific and less toxic drugs.

### Compendium of Hypotensive

Products containing Rauwolfia and/or its alkaloids, Rauwolfia contributions, Garglion Blocking Agents, Veratrum and Apresoline. Not included are the miscellaneous nitrates (marritol, erithyritol), thiocyarates, etc. since they are not the "newer drugs".

**HYPOTENSIVE PRODUCTS**

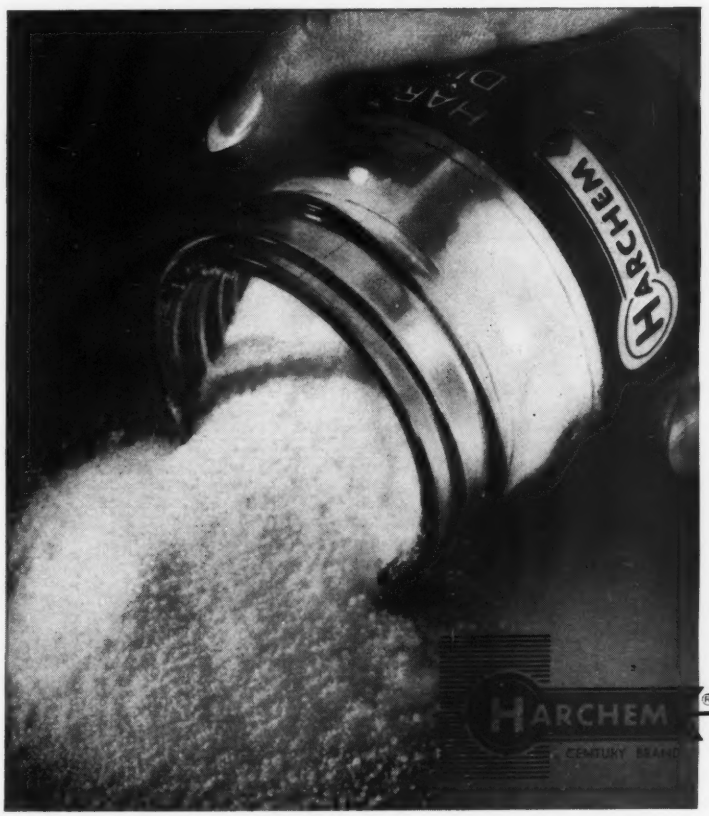
**Reserpine**

| Product | Mfgr. | Product | Mfgr. |
|---|---|---|---|
| Benasil | Ulmer | Serolfia | Ascher |
| Crystoserpine | Dorsey | Serpanray | Panray |
| Raurine | Lloyd | Serpasil | Ciba |
| Rau-Sed | Squibb | Serpena | Haog |
| Resercen | Central | Serpiloid | Riker |
| Reserpoid | Upjohn | Serpine | Pitman |
| Roxinoid | Merck-S.D. | Eskaserp | S. K. & F. |
| Sandril | Lilly | Spanzules | |
| Serfin | Parke-Davis | Resercen Timules | Central |

**ALSEROXYLON**
**(Alkaloidal Extract)**

| | | | |
|---|---|---|---|
| Rautensin | Dorsey | Rau-Tab | National |
| Rauwiloid | Riker | | |

(*Continued on page 542*)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**RAUWOLFIA**
**(Whole Root)**

| | | | |
|---|---|---|---|
| Koglucoid | Panray | Rauwoldin | Harvey |
| Raudixin | Squibb | Rauwistan | M. R. Thompson |
| Raupena | Crookes | | |

**RESCINNAMINE**
**(Chemically Pure Alkaloid Extract)**

| | |
|---|---|
| Moderil | Pfizer |

**RAUWOLFIA SERPENTINA COMBINATIONS**

| Product | Ingredients | Mfgr. |
|---|---|---|
| Rauvera | R. Serp. Alkaloid with Veratrum | Dorsey |
| Rau-Vertin | R. Serp. Alkaloid with Veratrum | National |
| Rauwiloid and Verloid | R. Serp. Alkaloid with Veratrum | Riker |
| Veralba-R | Reserpine, Protoveratrine | Pitman-Moore |
| Verapene | Reserpine, Protoveratrine | Wampole |
| Rauprote | R. Serp., Protoveratrine | Vale |
| Improved Potensors Forte | Whole Root Rauw., Veratrum Viride Alkaloids | Tailby-Nason |
| Vertina | Whole Root Rauw., Veratrum Viride Alkaloids | Elder |
| Verwolfia | Whole Root Rauw., Veratrum Viride | M. R. Thompson |
| Unitensin-R | Reserpine, Cryptenamine | Irwin-Neisler |
| Mio-Pressin | Whole Root Rauw., Protoveratrine Dibenzyline | S. K. F. |
| Raufia | R. Serp. Alkaloids, Verat. Viride, Marritol Hexanitrate, Rutin | Maney |
| Rau-Pertenal | Whole Root Rauw., Verat Viride, Marr. Hexanit., Homatropine Methyl Bromide | Crookes |
| Serpasil-Apresoline | Reserpine, Apresoline | Ciba |
| Methium with Reserpine | Hexamethonium, Reserpine | Warner-Chilcott |
| Pentoxylon | Alseroxylon, Erythritol Petranitrate | Riker |
| Nitralox | Alseroxylon, Pentaerythritol | Dorsey |
| Nitranitol R. S. | R. Serp. Alkaloids, Mannitol Hexanitrate | Merrell |
| Maxitate with Rauwolfia | Whole Root Rau., Mannitol Hexanitrate, Rutin | Strasenburgh |
| Glytheonate with Pheonbarbital and Rutin | Reserpine, Theophylline sodium Glycinate, Phenobarbital, Dihydroxy Aluminum Aminoacetate | Patch |
| Neo-Semhyten | Reserpine, Mannitol Hexanitrate, Theophylline, Rutin, Ascorbic Acid | Massengill |
| Loten Encotes | Rauw. Alkaloids, Neothylline, Rutin | Maney |
| Rutaminal-RQ | Reserpine, Aminophylline, Ascorbic Acid, Quercetin | Schenley |
| Theominal R. S. | Alseroxylon, Theobromine, Puminal | Winthrop |
| Theobarb-R | Reserpine, Theobromine, Phenobarb | Vanpelt |
| R-S Thesodate | Reserpine, Ascorbi Acid, Quercetin | Brewer |
| Sandril with Pyronil | Reserpine, Pyronil | Lilly |

**GANGLIONIC BLOCKING AGENTS**

| Product | Ingredients | Mfgr. |
|---|---|---|
| Etamon Chloride | Tetraethyl Ammonium Chloride | Parke-Davis |
| Priscoline | Benzazoline | Ciba |
| Esomid | Hexamethonium | Ciba |
| Hexameton | Hexamethonium | Burroughs-Wellcome |
| Methium | Hexamethonium | Warner-Chilcott |
| Bistrium | Hexamethonium | Squibb |
| Ansolysen | Pentolinium Bitartrate | Wyeth |
| Ilidar | Azopetine | Roche |
| Dibenzyline | Phenoybenzamine HCl | S. K. F. |
| Hydergine | Methanesulfonates of dehydroergocornine, dehydroergocristine dehydroergokrystine | Sandoz |
| Ecolid | Chlorisondamine Citrate | Ciba |
| Inversine | Mecamylamine HCl | Merck-S. D. |
| Arfonad | Trimethaphin camphor sulfonate | Hofmann-La Roche |
| Vertavis-Phen. | Veratrum Viride, Phenobarb | Irwin-Neisler |
| Veriloid | Verat-Veride | Riker |
| Verostan | Verat-Veride | M. R. Thompson |
| Veriloid V. P. | Veriloid, Phenobarb | Riker |
| Vergitryl | Verat-Veride | Squibb |
| Pertenol | Verat. Viride, Phenobarb, Mannitol Hexaanit | Crookes |

| | | |
|---|---|---|
| Nitranitol P. V. | Verat Alka'oids, Phenobarb, Mann. Hex. | Mervell |
| Veratrabar | Verat Alkaloids, Phenobarb, Mann. Hex. | Dorsey |
| Veriloid VPM | Verat Alkaloids, Phenobarb, Mann. Hex. | Riker |
| Vernite | Verat Viride, Phenobarb, Homat, Me Br. | Stoddard |
| Veratrite | Verat Viride Phenobarb, Sodium Nitrate | Irwin-Neisler |
| Veralba | Protoveratrines A and B | Pitman Moore |
| Raytrote | Verat Viride, Phenobarb, Nitroglycline | Raymer |
| Raytrote w Rutin | Verat Viride, Phenobarb, Nitroglycline, Rutin | Raymer |
| Veraflex | Verat Viride, Phenobarb, Nitroglycline, Rutin | Irwin-Neisler |
| Verutamin | Verat Viride, Phenobarb, Amenophyllin, Rutin | Adams |
| Provell | Protoveratine A and B maleates | Lilly |
| Potensors | Sodium Nitrate, Tet. Aconite, Verat. Viride | Tably-Nason |
| | **MISCELLANEOUS** | |
| Apresoline | Hydralazine | Ciba |

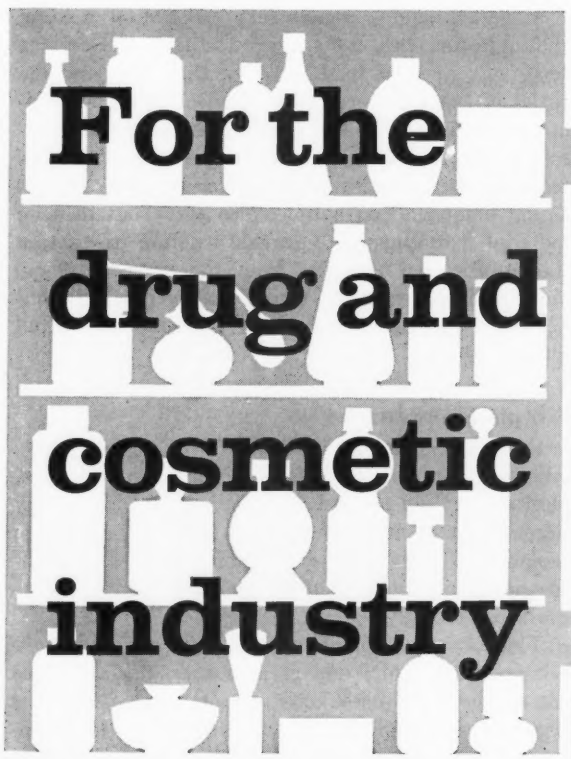
## LET ULTRASONICS HELP YOU

(*Continued from page 457*)

### Vibrator Head

The actual liquid whistle, or vibrator head, consists of the jet nozzle, with its slit-shaped opening and, immediately opposite it, the sharp-edged vibrating blade, all enclosed in an easily removable tubular housing, acting as a resonance chamber for concentrating the vibrations and imparting them effectively to the liquid. A sanitary inspection union in the vibrator head permits quick inspection or change of the blade, which is the only wearing part. It will last from several weeks to several months, and is both inexpensive and easy to replace. The action in the ultrasonic vibrator head, being vortex free, neither aerates, nor heats the product (except for the normal very slight temperature rise through the gear pump). Avoiding aeration increases stability, because the emulsifying agent tends to migrate to the liquid-air interface. Air entrapment also often causes indesirable side-effects leading to break-down of an emulsion. Ultrasonic homogenization also ensures a smooth texture and consistency, entirely free from lumps and usually with a glossy sheen which lends extra appeal to many products.

Fine variations in blade frequency are possible by a very simple and easy adjustment in the vibrator head which consists of varying the unsupported part of the blade by moving its four packing pieces either forward or backward. For average viscosity products the best setting has been found to be that which leaves the maximum part of the blade unsupported and free to vibrate, giving highest amplitude, equivalent to lowest frequency, at a pump output pressure of approximately 200 lbs. per square inch, observed from the pressure gauge fitted between pump and vibrator head. For very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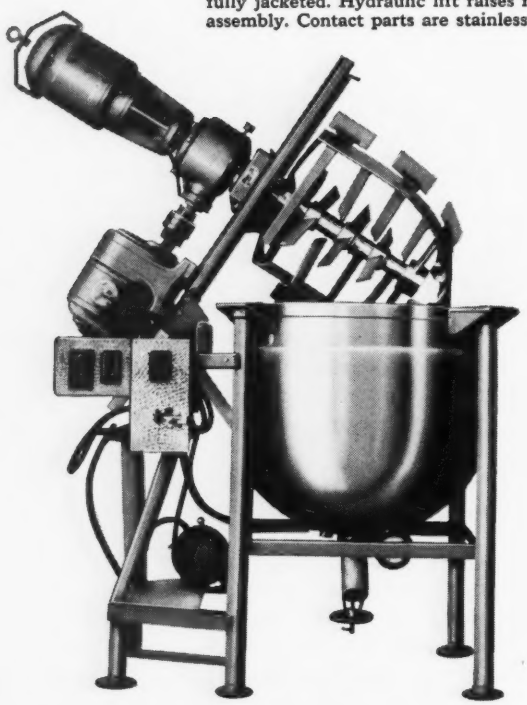

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viscous products a larger jet nozzle is often used to keep the pump output pressure down to 200 lbs. per square inch.

It is not necessary to prepare a premix of the ingredients. In emulsion-making, all oil solubles can be added to the oil phase and all water solubles to the aqueous phase, and the two phases can be introduced through two separate inlets on the pump and can therefore be varied with valves to the correct required ratio.

A further method is recirculation, which is sometimes preferred for difficult emulsions of light viscosity, when the unit will feed back into the same vessel.

Additional mechanical stirring is advisable in that case, and, by the law of diminishing returns, the whole amount will eventually have passed through the ultrasonic head once or several times, depending on the time recirculation is continued, the optimum being a matter of experimentation for each individual product.

### Typical Installation

The processing industries are becoming increasingly aware of the benefits of "ultramogenizing" and "ultramulsifying", as they have come to call this new process, using the simpler and more easily memorized contraction of "ultrasonically homogenizing" and "ultrasonically emulsifying".

In a typical installation the unit is connected to draw straight from the pre-mixing vessel or steam-jacketed mixing kettle. When all ingredients have been added, and the necessary amount of heating and agitation has been applied, the outlet of the kettle is connected to the inlet of the pump and the outlet of the vibrator head is connected to the holding or filling vessel, so that the ultrasonic unit becomes part of a continuous flow process. It will be seen that this unit will therefore—apart from the actual homogenizing action—also carry out its own material handling, i.e. provide suction to obtain the unprocessed material from the previous stage, and provide pressure to dispose of the finished product into the next stage which is usually the final filling stage.

### Simple Maintenance

It is of particular interest to processing plants where absolute cleanliness is of first consideration, that all parts in contact with the product are easily accessible and made of stainless steel for maximum sanitation. The unit is suitable for in-place self-cleaning, by running through with a soap or detergent solution.

There are few plants which have an abundance of space available, and it is noteworthy that this ultrasonic unit uses only about one-twelfth the space and one-fifth the h.p. of conventional homogenizers of equivalent output, and, furthermore,

it does not require water cooling, as frictional heat is practically absent. The weight of a complete machine is less than 140 lbs. so that the unit—which operates vibration free—can easily be made portable by mounting on a wheeled stand or by suspension from an overhead rail, to save space and permit easy transportation throughout the plant. It should also be mentioned that the vibrator head operates with full efficiency in any position including upward flow.

### Laboratory Model

A laboratory and pilot plant model is available for experimental work or small batch production. It includes two concentric funnels to feed-in the continuous and disperse phases of an emulsion, either separately or as a premix. It will handle anything from a pint to 40 gallons per hour and is driven by a ¾h.p. single phase motor. A recirculation hose is provided if more than one pass are beneficial. Any processing technique developed with this laboratory model can be reliably projected, without alteration, into full scale production.

### Cosmetics and Pharmaceutical Applications

With a machine that has proved its efficiency in homogenizing, emulsifying, dispersing and intimate mixing of both, lubricating and abrasive products, from free-flowing to heavy viscosities, the field of application has few limitations. The following applications will give some guidance to those who are considering this ultrasonic method for their cosmetics or pharmaceutical manufacturing or processing operations:—Baby lotions and creams, hand and face lotions and creams, deodorant creams, hair dressings, shampoos, liquid cleansers, waving and setting lotions, shaving cream, hormone lotions and creams, medicinal jellies, CMC dispersions, mucilages, fish liver oil emulsions, cough syrups, vitamin preparations, tonics, laxatives, dispersions, suspensions.

Almost every week new applications are being tried and frequently added to this ever growing list. To the cosmetics and pharmaceutical industries this new ultrasonic method and production equipment is the first decisive change and really big step forward since conventional piston homogenizers and colliod mills first took their place alongside the simple rotary mixer. It has brought increased efficiency by faster output, lower power consumption, negligible maintenance and lower capital investment.

There is no longer any doubt that both, small and large cosmetics and pharmaceutical manufacturers stand to gain a great deal in their existing production and in their development of new products by taking a close look at their present methods and comparing them with the many advantages of mechanical ultrasonic processing.


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*(Continued from page 447)*

cation? If the Secretary refuses to permit the change, is there any ground for appeal? Even more basic, does the Secretary have authority to refuse to permit the change, and, if so, what are the limitations upon this authority?

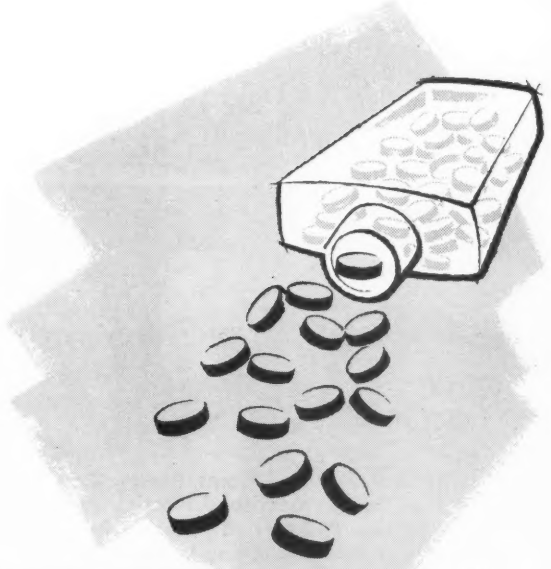
No hint of an answer is found in the statute or the regulations. Is he then at the mercy of whimsical decisions regarding subsequent changes? One way of avoiding this result might be to file a new application to which all the procedural safeguards set forth in new drug section of the Act would attach. However, it appears that the gerneral practice is to file what regulations call a "supplemental application" merely setting forth the changes to be made. Although supplements to applications far outnumber original ones, and provide the reason for most frequent contacts with the Administration, no major difficulties appear to have been encountered under the system. In everyday practice, the Administration has acted speedily and with sympathetic consideration of the facts. Indications are that the Administration assumes the same responsibilities in regard to supplements as it does in regard to original applications. Although the rights and duties of the parties are not defined by the statute, it would seem that the practice which has developed has proved satisfactory to government and industry.

Suppose that the label of the original product contained the prescription legend, and it now appears that the product should be sold over-the-counter. A 1951 amendment to the statute provides that a drug for use by man which is restricted by an effective application to use under professional supervision may be dispensed only in certain designated ways on prescription. It further provides that the Administration "*may by regulation*" remove such drugs from this restriction. Regulations were promulgated in December, 1951 to prescribe a method by which removal of the restriction could be accomplished. Under the regulations, the proposal for change may be in the form of a supplemental application, but "any interested person", including the Secretary, may propose such a change. Submission of views upon a controversial proposal is provided for. This procedure appears to conflict with the usual approach in which the applicant presents data privately to the Administration whose function it is to review and advise—not to affirmatively act on its own behalf, placing the applicant in a defensive role. Furthermore, the procedure appears to remove the proprietary interest one usually gains through clinical research regarding the safety of new drugs. In addition, no procedural safeguards are set forth, and, as was noted before, it is not clear whether a supplemental application is entitled to the safeguards surrounding new drug applications.

The statute does not state that the promulgation of regulations is the only way by which the restriction of a new drug to prescription dispensing may

be removed. It is merely one of the ways by which the restriction could be removed. For more than three years following enactment of the Amendment which permitted the Administrator to remove prescription dispensing requirements by way of regulation, no such regulations were published, and the legend was removed from a number of new drug products with official sanction. This was done by appropriate amendments to effective new drug applications on an individual basis. However, regulations now provide that a drug restricted by its new drug application to prescription dispensing remains so restricted until exempted under the rule-making process. Notice that this regulation only applies to drugs already restricted by effective applications and, presumably, would not apply to an original new drug application in which over-the-counter marketing is proposed.

Therefore, our fictional applicant might have two alternatives, (1) file a supplemental application suggesting such a change, or (2) file another new drug application which sets forth labeling under which the product could be sold without a prescription. The latter procedure might avoid the cumbersome rule-making machinery as well as provide the procedural safeguards set forth in the new drug provisions. However, it does not appear that such a procedure has been attempted to date in an effort to avoid the rule-making procedure, and the attitude of the Administration toward it is unknown. The Administration might oppose it in that the avowed purpose of the presently used rule-making process is to achieve uniformity in the marketing of identical products. Whether uniformity will result is met with a question mark since it appears that a manufacturer who is dissatisfied with an exempting regulation might be able to avoid its effect. Regulations setting forth the exempting machinery provide that a drug exempted under them may not be labeled with the prescription legend. The exempting regulations provide the terms under which exemption is gained; e.g., statements of indications, dosage, and/or warnings that must be placed on the label. If a product does not bear the statements prerequisite to exemption, obviously it is not exempted from the prescription dispensing requirements required by its effective new drug application. Situations have already developed where a product's uses are restricted by the exempting regulations for purposes of self-medication but the basic application recognizes that the same product may be used safely under medical supervision for many other uses and it is so promoted by the manufacturer to physicians. In such cases, must the manufacturer market the product under two types of labeling—one bearing over-the-counter labeling, and the other bearing the prescription legend? Or may the manufacturer select either of the two types of labeling to be employed? These questions as well as the more basic ones concerning the procedure for changing the marketing of a drug

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from prescription dispensing to over-the-counter, are as yet, unanswered.

Though the road has been bumpy, and washed out in places, our applicant has finally arrived, or so he thinks. His sales and advertising groups are now ready to contact the market. At this point the following questions arise: What control does the government have over product promotion and advertising? Must advertising matter be cleared with the F.D.A.? What promotional statements may be made for the product. What warning statements, if any, must be set forth in advertising? Some of these problems were recently described by the Administration's Medical Director as going to the very heart of the new drug procedure, and its underlying philosophy. Their importance is certainly admitted, for if conditions of use are not adequately known, the product may be either worthless or dangerous.

Under the new drug provisions, only labeling must be submitted for clearance. The cases, as you know, have extended the concept of "labeling" quite a long way, so that the term includes printed matter having textual relationship and common destination with the drug. Court decisions tell us this. Legislative history indicates that usually radio, newspaper, and magazine advertising are not labeling. However, newspaper or magazine advertisements might be considered as labeling if displayed with the drug at its point of sale.

In the case of ethically promoted drugs, promotional literature frequently does not have a common destination with the drug to which it refers since the literature is sent to physicians and the drugs to pharmacies. Furthermore, the purpose of the literature is to inform persons who supervise the use of the product; not those who use the product for themselves. These factors create additional doubts regarding the labeling status of such literature.

Whether a particular promotional piece must be submitted to the Administration for prior approval, depends upon its status as labeling. Advertisements that are not labeling need not be submitted. However, such advertisements are subject to the effective application. If an advertisement suggests conditions of use different from those stated in the application, proceedings might be instituted to revoke or suspend effectiveness of the application on the ground that it contains an untrue statement of a material fact. Furthermore, if the product is marketed over-the-counter and advertising sets forth uses for which adequate directions are not contained in labeling, the product will be misbranded. In each instance, however, fault would lie in stating different conditions of use, and not in merely using different words to express the same conditions of use.

Under the misbranding provisions, we find only one affirmative requirement as to the content of labeling, as distinguished from labels; that is, labeling must bear adequate directions for use and adequate warnings against use. A question that frequently

arises here is in regard to the labeling pieces that must bear such information. From the beginning, the section has not been interpreted to require that directions and warnings be placed in each piece of labeling. If directions and warnings are sufficiently prominent in certain pieces, it would seem that such information may be omitted from others. There are no hard and fast rules, however, for appraisal of the required prominence of directions or warnings, or selection of labeling pieces upon which such information must be stated, and it is doubtful if hard and fast rules would be workable. Each tub must sit on its own bottom. It is a matter to be judged according to the drug involved and the state of knowledge concerning its use. Again, it is an opportunity for industry-government cooperation.

Throughout, an attempt has been made to limit examples to those that seem basic. Hundreds of details could be mentioned where manufacturers go beyond the call of duty in satisfying the suggestions of their advisors in the Food and Drug Administration. Although legal support may be lacking, agreement is reached on what is necessary, proper, and workable in protecting public health in the manufacture and marketing of drug products.

Lawyers naturally cherish the values of certainty and security in the law. However, changes in the drug industry are so swift and their effects so devastating upon past principles, that static, settled rules for regulating drug manufacture and distribution may be more burdensome than appropriate.

Furthermore, significant changes are not the sole province of science. The average consumer today is better educated, more urban, more persceptive, and management is more aware of its public responsibilities. The effects of these social changes affect the constantly shifting balance between freedom from control on the one hand and adequate regulation for public protection on the other. Regulation which co-mingles social and scientific concepts must be flexible in order to keep pace with the subjects and beneficiaries of its rules.

The fact that the true meaning of drug regulations under the Federal Food, Drug and Cosmetic Act does not reside in its language is not a fault. That drug regulation is more to be felt than understood is only a natural result of a free competitive society encouraging vast medical research. The kinds of problems created by the fruits of this research are welcomed: How sad we would be without them. There is another lesson in all this, and it is that neither government nor industry can afford to maintain an uncompromising position, particularly through extreme statutory interpretations. The fact that a right exists by statute to make or market a drug product in a particular manner may not be a good reason or excuse for its exercise. The fact that the statute permits the Administration to forestall a plan of manufacture or marketing, likewise


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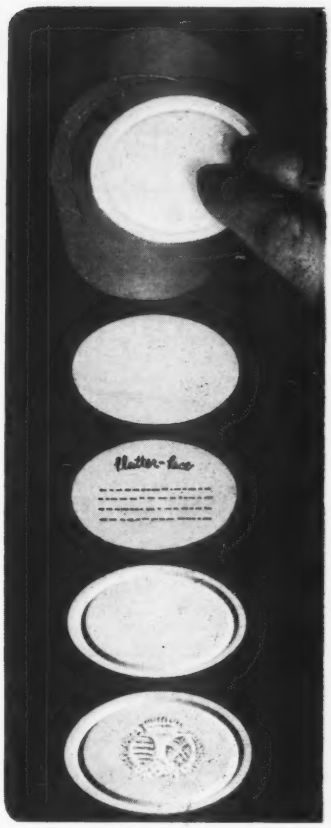

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might in certain circumstances better be waived.

An improvenent in the control of drug products under the Federal Food, Drug and Cosmetic Act is not to be found in a proliferation of detailed regulations, but in testing each problem as it arises against the basic philosophy of the statutory scheme. This philosophy is the encouragement of conditions conducive to successful manufacture and marketing of safe and sound drug products.

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## ORAL DIABETIC DRUGS

(*Continued from page 518*)

Seventy-five adult diabetics have been observed on tolbutamide (Orinase) therapy for periods up to one year by *S. Sherry*. The remaining 57 patients are still under observation. They have all shown a good or partial response to tolbutamide therapy as judged by such criteria as the fasting blood sugar, post-prandial blood sugar rise, and glycosuria. Approximately 90 per cent of the patients with a good or partial initial response have maintained their response over the entire period of observation. In the remaining 10 per cent, the patients have either not maintained as good a response or have become unresponsive to oral therapy. In seven of the patients who had maintained a good response for six months or longer, tolbutamide was replaced by a placebo. Five of these latter patients promptly had a worsening of their control. The other two are still under observation on the placebo.

Hematologic study (blood and platelet counts) and hepatic function tests (BSP, prothrombin time, total proteins, A/G ratio, alkaline phosphatase, cephalin flocculation) were performed at frequent intervals. No significant evidence of hepatotoxicity or hematologic dysfunction have been observed in the patients to date.

On 174 patients in the metropolitan area of Washington, D. C., treated with Orinase by *S. J. N. Sugar*, 75 per cent were well controlled with an average maintenance of one gram per day.

Side-reactions were not too severe as a rule. Prominent was a tendency to gain weight observed in a third of patients. One case of leukopenia with a white count of 1800 was noted. This was not permanent and Orinase was resumed without ill effect. One case of itching and purpuric rash was severe enough to warrant discontinuing the drug.

Most easily controlled with Orinase were middle aged patients with relatively recent onset of diabetes requiring less than 40 units of insulin.

A group of 90 tolbutamide treated diabetic patients have been under constant observation by *S. B. Beaser* some for up to 10 months. Initial stabilization of the tolbutamide dose occurred in the first 3-5 weeks of therapy. The integrity of islet function is not affected

by tolbutamide therapy in the first six to 10 months.

The unfavorable effect of tolbutamide upon those with a susceptible upper gastrointestinal tract is reported. It should be used with antacids in those with known gastric or duodenal ulcer or suggestive symptoms.

Thyroid function as measured by the clinical condition and by serum protein bound iodine, basal metabolic rate and thyroidal uptake of radioiodine has been studied by *T. H. Gavack et al.* in 55 subjects receiving carbutamide (27 subjects), tolbutamide (28 subjects) and both consecutively (13 subjects).

A statistically significant decrease in radioiodine uptake was observed when two grams of the drug were used daily. Despite continuance of the drug at the same level of dosage these values had returned to normal or above at the end of 22 weeks. When tolbutamide was administered in doses of one and two grams daily, respectively, no changes in any of the indices of thyroid function were recorded over periods of time up to 47 weeks.

Continuous personal observation of over 500 diabetic patients treated with Orinase on an ambulatory basis serves as the basis of a report by *H. Dolger*. The experience extends over one year of treatment.

Toxicity and side reactions occur in less than one per cent of treated cases and consist mainly of transient skin reactions. No significant disturbance of the hematopoitic, hepatic or renal systems is demonstrable.

The general impression of the overall experience indicates that Orinase can be used successfully in the treatment of 70 per cent of all adult patients, replacing the insulin in about one-half of those using it heretofore.

## AEROSOL PACKAGING

*(Continued from page 469)*

are stabilized by the use of proper emulsifying agents. In the valve, the propellent evaporates. This separates the water droplets to produce a fine spray.

The emulsifying agent used is a nonionic, oil-soluble material, and there is very little or no foaming either at the valve or on a sprayed surface.

Although this development is so new that no aerosol products of this type have yet been marketed, we can expect to see a number of products based on this system in the near future. These may include personal products such as antiperspirants, deodorants and depilatories, hair tints and hair waving solutions, and household products such as glass and metal cleaners, stain removers and adhesives. These products have not been entirely practical in in other aerosol systems.

Regardless of the technical details needed to achieve successful aerosol packaging, let me conclude by summarizing the major incentives for trying. Five of these reasons, with an example of each are:


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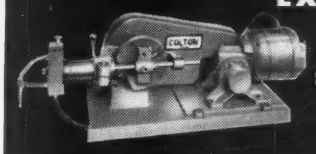

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3. **HIGH SPEED OPERATION**—zips out sample batches—fast.
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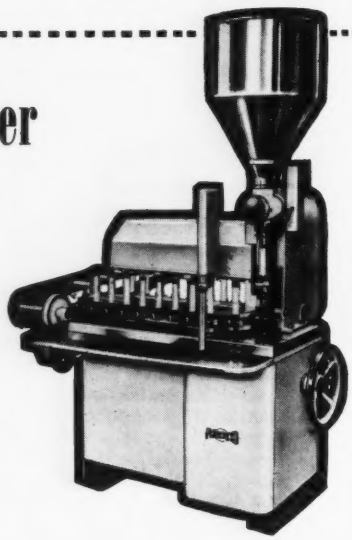

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Actually, most successful aerosol products combine several of these advantages over the corresponding nonaerosol product. There is a very large market potential for well-formulated aerosol products which serve a real consumer need.

## ANTIBIOTIC CONSIDERATIONS IN THE COSMETIC AND ALLIED FIELDS

(*Continued from page 460*)

application" form provides guidance for the requirements to be met before the product is marketed. The application form is obtainable from the Department of Health, Education and Welfare, Food and Drug Administration, Washington, D. C.

For convenient guidance the form outlines and describes detailed requirements of investigations dealing with safe use of the drug, listing of formula and composition, methods of manufacture and packaging, submission of samples, copies of labeling, statement of how product is intended to be used, and provision for supplemental application.

Cosmetic manufacturers as a whole should have no difficulty in carrying out the provisions required. Most of the requirements cover details already in possession of the manufacturer when cosmetic products are in the process of being considered or evaluated for marketing.

Those cosmetic manufacturers having scientific and/or suitable outside consultant contacts as well as adequate laboratory and library facilities would be in a position to accumulate "reports of all investigations that have been made to show whether the drug is safe for use." Similar or approximate investigations are often probably routine with the cosmetic manufacturer anyhow.

Table No. 10 conveniently indicates whether a "nda" is required for the antibiotics discussed herein.

The incorporation of tyrothricin in products probably would require a "new drug application" to be submitted before marketing, although there are instances where the "nda" procedure may not be required; for instance, in certain products where tyrothricin is the sole active ingredient (except for benzocaine), such as in a throat lozenge.

To include tyrothricin in a cosmetic product at the present time probably would require prior submission of a "nda." Neomycin would require a "nda" before marketing is permitted.[2]

Bacitracin is a "certifiable" antibiotic and products containing this drug require certification (application) with the Division of Antibiotics, Food and

Drug Administration; but for use as a pharmaceutical product the plain ointment of bacitracin has been de-certified, although such ointment is still subject to prior Food and Drug Administration approval before marketing.[1] Certification is largely similar to the "nda" procedure and details are obtainable from the Division of Antibiotics.

The fact that a product may require a "nda", or certification, does not necessarily mean that it cannot be sold over-the-counter without prescription. It would depend upon the nature of the antibiotic. Obviously the inclusion of potent antibiotics such as penicillin, streptomycin, chloramphenicol, the tetracyclines, etc. in products are required to be dispensed only on prescription.

Tyrothricin, neomycin and bacitracin oftentimes can be incorporated in products permissible for sale without prescription. Apparently the main reason why these particular antibiotics are permitted for use in certain over-the-counter products is because of the documentary evidence that they are safe agents when used as indicated.

### Summary

Tyrothricin, neomycin and bacitracin, along with their derivatives or extractives, represent a selective small group of antibiotics which could qualify as suitable active agents in cosmetic and allied products.

Tyrothricin (or its extractive gramicidin) is presently the major antibiotic potential in this field. Neomycin's potential is second only to tyrothricin and is dependent on accumulation of more data to demonstrate its acceptability.

The newly developed salt, neomycin palmitate, may be of specific interest.

The potential of bacitracin is related to its bactericidal gram-positive action against skin bacteria, and is also dependent on accumulation of more data to demonstrate its acceptability.

**Literature**

1. W. B. Shelley and M. M. Cahn. Effect of Topically Applied Antibiotic Agents on Axillary Odor. J. A. M. A., **159:** 1736, (Dec.) 1955.
2. W. B. Baker. Aspects of Several Antibiotics. Drug and Cosm. Ind., **75:** 764, (Dec.) 1954; **76:** 46, (Jan.) 1955; **76:** 178, (Feb.) 1955.

## WOOING THE DOCTOR THROUGH CLOSED - CIRCUIT TV

*(Continued from page 547)*

feature article which appeared the day following the telecast estimated that 10,000 physicians in the sixteen cities saw the program, with well over 3,000 doctors and their wives in The Shrine Auditorium.

On April 10, originating in Chicago, "The Fight For A Free World" was produced. This time twenty-two Midwestern cities were on the closed-circuit cable. The program presented General Collins and Leon Keyserling, famed economist and former

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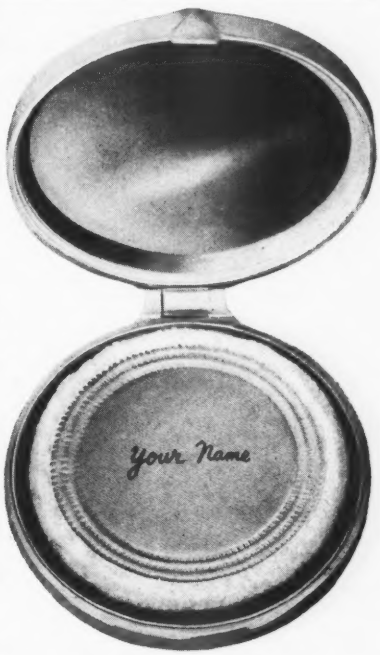


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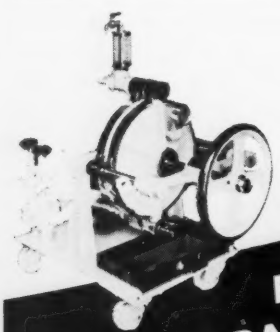

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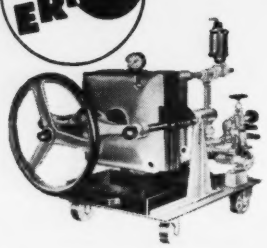

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Chairman of the President's Council of Economic Advisors. Two ex-communist secret police members were also on the program. Once again Mr. Spivak was program moderator, and presented a distinguished panel of newsmen.

Basically, Pfizer has found that these programs do a great deal towards bringing the physician closer together with Pfizer and Roerig representatives. They meet, talk and generally get acquainted on a completely different basis than is possible when the detailman ordinarily calls on the physician. Thus far, there has been no use of the television series to present any commercial message from Pfizer. However, the invitations display the Pfizer-Roerig names, and the TV program opened and closed with an institutional announcement featuring Pfizer and Roerig.

Pfizer reports that these programs have been very well received by physicians. Letters and personal comments at the various reception points have encouraged the company to consider the possibility of additional closed-circuits in the coming months.

Mr. O'Toole has said, "We have found that by tying together several cities on one night for one hour, we not only can get physicians together, but are able to get internationally known authorities to appear as guests on the programs. These experts with their comprehensive commitments would never be available for a series of 20 individual appearances before medical societies. With the use of closed-circuit we are able to provide exciting programs for local medical societies that would be impossible to produce on a city by city basis."

---

## RECENT PATENTS

*(Continued from page 483)*

**trinsic Factor Preparation of Enhanced Potency.**

*2,770,572*—**Nordisk Insulin (Denmark) — Blood Grouping Card.**

*2,770,573*—**Am. Home Products—Enzymatic Synthesis of N-Acetylglucosaminido Galactose.**

*2,770,575*—**J. Lyons & Co.—Bacterial Enzyme Preparations and Cultivation of Microorganism of Industrial and Nutritional Value.**

*2,770,599*—**Colgate-Palmolive — Stable Liquid Shampoos.**

*2,770,600*—**Colgate-Palmolive — Particulate Detergent Compositions.**

*2,770,616*—**Protein Foundation—Fractionation of Proteinaceous Materials in Blood Plasma and Liver Tissue.**

*2,770,617*—**Ciba Pharmaceutical—2,5-Bis-Ethyleneimino Hydroquinone.**

*2,770,618*—**Am. Home Products—Tomatidines.**

*2,770,619*—**Schenley Industries—Substituted 8-Quinolinols.**

*2,770,624*—Gohei Tanabe (Japan) — Thiamine Salts.
*2,770,627*—Ciba Pharmaceutical—Deserpidinol.
*2,770,646-7*—Schieffelin — Quat. Ammonium Compounds of Basic Esters of 2-aryl-2-(1-Hydroxycycloalkyl) Ethanoic Acids.
*2,771,391*—Allied Labs.—Physiologically Active p-Alkoxy-Beta-Piperidinopropiophenones Causing CNS Depressant and Anesthetic Effects in Animals.
*2,771,392*—Chas. Pfizer—Carbomycin Complexes.
*2,771,393*—Chemie et Atomistique (France)—Desoxybenzoins.
*2,771,394*—Colgate-Palmolive — Hair Grooming Preparation.
*2,771,395*—Colgate-Palmolive — Aqueous Alcoholic Hair Grooming Preparation Employing Sodium Carboxymethyl Allulose.
*2,771,397*—U.S.A.—Polymyxin.
*2,771,398*—U.S.A.—Apparatus for Counting Microorganisms.
*2,771,399*—Upjohn—Apparatus for Determining Biological Potency of a Substance in a Liquid Substrate.
*2,771,467*—Upjohn—Steroid Ketals.
*2,771,468*—Sterling Drug—4-Aralkyl-3-Morpholones.
*2,771,469*—Merck—Quat. Ammonium Salts of Delta - Hydrocarboxyphenyl Gamma - Hydroxy Amines.
*2,771,475*—Upjohn—Steroids.
*2,771,476*—Upjohn — 11alpha - Acyloxy - 17alpha-Halo-4-Pregnene-3,20-Dione.
*2,772,168*—Colgate-Palmolive—Permentable Carbohydrate Food Products.
*2,772,201-2*—Am. Home Products — Recovering Diphtheria and Tetanus Toxoids.
*2,772,268*—Wm. S. Merrell Co.—Spiro Cycloalkane-Thiazaneones.
*2,772,270*—M. J. Lewenstein — 14 - Hydroxymorphinone.
*2,772,286*—Eli Lilly—Epoxybenz (CD) Indoles.
*2,772,287-9*—G. D. Searle—Basic Esters of N-Aralkyl- and N-Aryl-N-Carbamic Acids.
*2,772,298*—G. D. Searle—11-Oxygenated Derivatives of 13-Methyl-Tetradecahydro-15H-Cyclopenta (a) Phenanthrene-3,17-Dione.
*2,772,299*—Upjohn—4-Chloro-11alpha, 17alpha-Dihydroxypregnanes.
*2,772,300*—Merck—Dithio-Dioctanoic Acids.
*2,772,303*—E. A. H. Friedheim—Therpaeutic Organometallic Compounds Containing Antimony and Sulfur.
*2,772,998*—J. A. Benckiser (Germany)—Choline Salt Tablet.
*2,772,999-3,000*—Johnson & Johnson — Hemostatic Surgical Compositions and Dressings.
*2,773,058*—Am. Cyanamid—Delta$^4$-Pregnenes.
*2,773,059-60*—Upjohn—Steroid Ketals.

*(Continued on page 556)*

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*2,773,064*—Parke, Davis—7-Substituted Amino-Benz [c] Acridines.

*2,773,065*—G. Carrara (Italy)—Cycloalkanone-carboxylic Acid Isonicotinylhydrazones.

*2,773,068*—H. S. Mannheimer—Substitution Derivatives of Imidazoline Alkanoic Quat. Ammonium Hydroxide.

*2,773,069*—Upjohn—Amines.

*2,773,073-9*—Syntex S.A. — Cyclopentanophenanthrene.

*2,773,075*—Merck—Allopregnenes.

*2,773,076*—Organon — Compounds having Adreno-Cortical Hormone Activity.

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*2,773,091*—G. D. Searle — Fluorantheneoxocarboxylic Acids.

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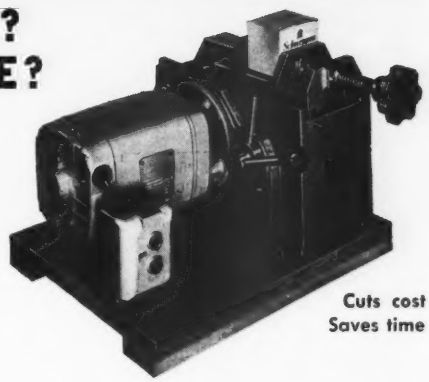

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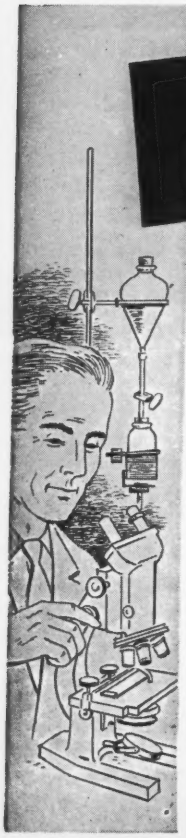

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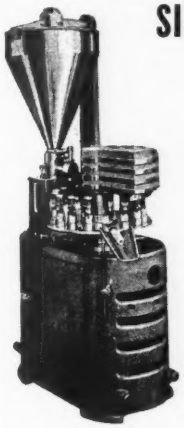

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